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Original Communications

RADICAL HYSTERECTOMY AND PELVIC LYMPHADENECTOMY*

A Review of 473 Cases Including 244 for Primary Invasive Carcinoma of the Cervix

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THE purpose of this study was twofold: (1) to analyze certain clinical aspects of patients suffering from cancer of the uterus or vagina who had radical hysterectomy with pelvic lymphadenectomy, and (2) to review the result of surgical treatment for carcinoma of the cervix.

Material and Method

The material is based upon a series of 473 cases of radical hysterectomy with pelvic lymphadenectomy, performed by the staffs of the Vincent Memorial Hospital, the Massachusetts General Hospital, the Pondville Hospital (Massachusetts Department of Public Health) and the Palmer Memorial Hospital during a period of almost fifteen years, from February, 1939, to December, 1953. Both clinic and private patients were included. The operative procedure was that described by Meigs.[1] In cases of carcinoma of the cervical stump or carcinoma of the vagina after a previous total hysterectomy, the procedure was similar, with the radical removal of the broad ligament, paracervical and paravaginal tissue, and pelvic lymph nodes. In cases of carcinoma of the cervix the clinical extent of the tumor was grouped according to the International Classification.

The data will be presented in two parts: (1) general information on patients who had radical hysterectomy with pelvic lymphadenectomy, and (2) radical hysterectomy with pelvic lymphadenectomy as a treatment for carcinoma of the cervix.

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PART I. GENERAL DATA ON ALL CASES TREATED BY RADICAL HYSTERECTOMY WITH PELVIC LYMPHADENECTOMY

1. Yearly Distribution.—

There were 473 operations of radical hysterectomy with pelvic lymphadenectomy performed between February, 1939, and December, 1953. Two hundred fifty-four patients were clinic and 219 were private. Approximately two-thirds of the operations were performed between 1948 and 1953. The yearly distribution as well as the number of clinic and private patients is shown in Table I.

TABLE I. YEARLY DISTRIBUTION OF 473 CASES OF RADICAL HYSTERECTOMY

YEAR	CLINIC PATIENTS	PRIVATE PATIENTS	TOTAL PATIENTS
1939	3	0	3
1940	10	2	12
1941	7	2	9
1942	15	4	19
1943	12	7	19
1944	9	10	19
1945	16	4	20
1946	16	6	22
1947	15	19	34
1948	20	37	57
1949	33	24	57
1950	24	30	54
1951	22	32	54
1952	31	24	55
1953	21	18	39
Total	254	219	473

TABLE II. TYPES OF TUMORS IN 473 CASES OF RADICAL HYSTERECTOMY

Primary cancer of the cervix		322
Squamous-cell carcinoma	294	
Adenocarcinoma	27	
Leiomyosarcoma	1	
Primary carcinoma of the cervical stump		23
Squamous-cell carcinoma	21	
Adenocarcinoma	2	
Primary carcinoma of the corpus		47
Primary carcinoma of the vagina		5
Recurrent or residual carcinoma of the uterus		21
Squamous-cell carcinoma of the cervix	18	
Adenocarcinoma of the corpus	3	
Carcinoma in situ of the cervix		34
Referred cases (Cancer in preliminary biopsy but no cancer in surgical specimen)		21
Total		473

2. Types of Tumor.—

The malignancy in this series of 473 cases was distributed as follows: 294 cases of primary squamous-cell carcinoma of the cervix, 27 primary adenocarcinoma of the cervix, 1 leiomyosarcoma of the cervix, 23 carcinoma of the cervical stump, 47 primary carcinoma of the corpus, 5 primary carcinoma of the vagina, 21 recurrent or residual carcinoma of the uterus, originally treated elsewhere with irradiation or surgery (18 cases were squamous-cell carcinoma of the cervix and 3 were adenocarcinoma of the corpus) and 34 cases of carcinoma in situ of the cervix. Twenty-one patients were referred

for radical surgery with a diagnosis of cancer of the uterus made at another hospital. Fifteen of these 21 patients had previous irradiation therapy, 2 had total hysterectomy, and 4 patients had no treatment except diagnostic procedures before referral. None of these 21 patients, however, had any residual cancer demonstrable in the surgical specimens removed at the radical surgery. These cases were therefore grouped separately (Table II).

3. Age Distribution.—

The age of these 473 patients ranged from 17 to 80 years. The peak incidence was in the late forties, as shown in Fig. 1.

Generally, patients suffering from carcinoma of the corpus are in the older age group. This was also true in the present small series. Of 47 patients with carcinoma of the corpus, 4 were between 35 and 44 years of age, 6 were between 45 and 49 years, 23 were between 50 and 59 years, 12 were between 60 and 69 years, and 2 were between 70 and 80 years.

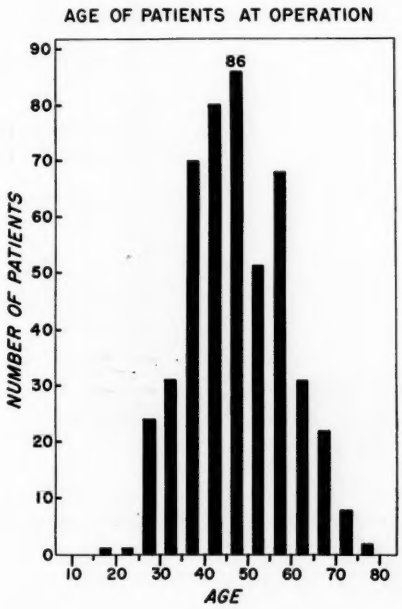

Fig. 1.

4. Age at Marriage.—

Of the entire series, 449 were married and 24 were single. Of the 255 patients in whom the age of marriage is known, 120 (47 per cent) had married before the age of 20.

Lombard and Potter[2] in their epidemiological studies of cancer of the cervix emphasized the relationship between early marriage and this disease. They have found that 44.6 per cent of individuals with carcinoma of the cervix had been married before the age of 20, in contrast to 23.7 per cent of the matched controls. They explained the possible causes of early marriage by poverty, unhappy home life, precocity and excessive sex urge, and the possible relationship between early marriage and cancer of the cervix by excessive hormonal stimulation, lack of development, and injuries to immature tissue in youthful marriages.

In the present study, 397 patients suffered from cancer of the cervix. Of these, 9 were single. Of the 245 cases in which the age of marriage was

known, 112, or 45.7 per cent, of the patients had married before the age of 20, the majority at age 18 (Fig. 2).

5. Symptoms.—

Symptoms of these patients varied from no complaint, or oligomenorrhea for six months, to a history of intermittent vaginal bleeding for a period of 11 years. The parity of these patients ranged from primary sterility to gravida xvii, para xv.

TABLE III. CONSTITUTIONAL DISEASES OF 399 PATIENTS WITH CARCINOMA OF CERVIX

Obesity	36	
Hypertension	35	(140/100 mm. Hg or more)
Ovarian cystectomy	19	
Syphilis	13	(2 with central nervous system involvement)
Previous bleeding and curettage	11	(1 or more years previously)
Thyroid disorders	11	(5 had thyroidectomy)
Psychiatric disorders	12	(7 before and 5 after operation)
Diabetes mellitus	9	
Benign breast tumor	7	
Gonorrhea	6	
Peptic ulcer	5	(1 had subtotal gastrectomy)
Asthma and hay fever	6	
Rheumatic fever	7	
Pulmonary tuberculosis	7	(1 had thoracoplasty)
Gall bladder disease	4	(2 had cholecystectomy)
Cervical polyp	4	
Empyema	3	(2 had rib resection)
Pleurisy	4	
Chronic cystitis	2	
Cirrhosis and alcoholism	3	
Partial amputation of cervix	2	(6 or more years previously)
Dermatitis	3	
Chorea	2	
Repeated pyelitis	1	
Double ureter and kidney, bilateral	1	
Nephrectomy	1	
Pelvic inflammatory disease	1	
Condyloma	1	
Coronary thrombosis	1	
Sciatica	1	
Fundectomy for fibroids	1	(13 years previously)
Second-degree prolapse of uterus	1	
Repeated severe toxemia during pregnancy	1	
Retroverted uterus with prolonged use of pessary	1	
Rhinoscleroma with tracheotomy for 19 years	1	
Pernicious anemia	1	

TABLE IV. CONSTITUTIONAL DISEASES OF 47 PATIENTS WITH CARCINOMA OF CORPUS

Hypertension	13	(140/100 mm. Hg or more)
History of bleeding, curettage	9	(1 or more years previously)
Psychiatric disorders	9	(4 before and 5 after operation)
Obesity	7	
Cervical polyp	4	
Diabetes mellitus	3	
Rheumatic fever	3	
Ovarian cystectomy	2	
Thyroid disorders	2	
Benign breast tumor	1	
Syphilis	1	
Cholecystectomy	1	
Nephrectomy	1	

6. Constitutional Diseases.—

The constitutional diseases as recorded in the clinical histories of 447 patients who had carcinoma of the cervix or the corpus are separately listed in Tables III and IV.

The frequent observation of hypertension, obesity, and diabetes in association with carcinoma of the corpus seems to hold true in this small series. Uterine bleeding, with single or repeated curettage one or more years prior to the diagnosis of malignancy, seems also to be an important item of the past history among patients with carcinoma of the corpus.

Twenty-one patients of the combined group had psychiatric disorders; 11 cases were recognized before the radical surgery, and 10 had their first manifestation during the early postoperative period.

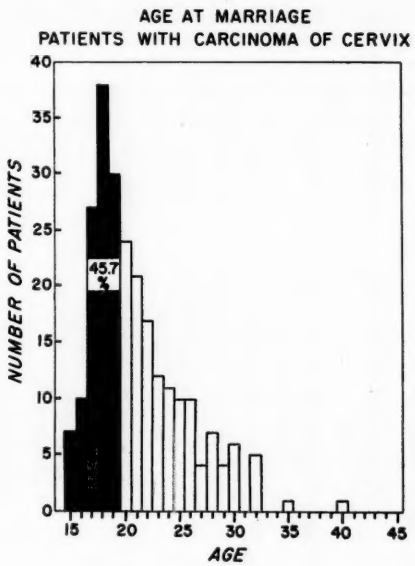

Fig. 2.

7. Pregnancy.—

Six of the 473 patients were pregnant at the time of radical surgery (Table V). Four had a Stage I squamous-cell carcinoma of the cervix complicating intrauterine pregnancies of 8 weeks' to 6½ months' duration. Of the other 2 patients, one had a Stage II squamous-cell carcinoma of the cervix with the incidental findings of decidua and chorionic villi in the surgical specimen, and one had carcinoma in situ of the cervix with the incidental finding of a tubal pregnancy. All 6 have been well from 3 to 11 years after the operation.

Patient No. 4 in Table V was particularly interesting.

She was 40 years of age, married at 17, gravida v, para v, with a chief complaint of metrorrhagia for one year. When first seen at the clinic, she had a Stage I squamous-cell carcinoma of the cervix and a gravid uterus of about 6½ months' size. Preoperative radiation therapy was given in the form of interstitial radium, 1,680 mg. hr. to the periphery of the cervix and 2,289 mg. hr. to the endocervical canal. Four weeks later a cesarean section was done and she was delivered of a 3 pound, 8 ounce live baby girl, with an area of alopecia at the presenting part (left occipitoanterior). The patient was subsequently operated upon and metastatic carcinoma was found in a right obturator

TABLE V. PATIENTS WHO WERE PREGNANT OR WITHIN ONE YEAR POST PARTUM

PATIENT	AGE	DURATION OF PREGNANCY	CANCER	PREOPERATIVE TREATMENT	NODES	OUTCOME
1. H. R.	44	8 weeks	Squamous ca. of cx., Stage I	X-ray followed by spontaneous abortion	-	Well 11 years
2. C. M.	38	2 months	Squamous ca. of cx., Stage I	None	-	Well 4 years
3. C. N.	26	4 months	Squamous ca. of cx., Stage I	None	-	Well 3 years
4. E. G.	40	6½ months	Squamous ca. of cx., Stage I	Radium, cesarean section	+	Well 11 years
5. J. P.	30	Incidental finding of decidua and villi	Squamous ca. of cx., Stage II	X-ray	-	Well 6 years
6. V. A.	38	Incidental finding of tubal gestation post partum	Carcinoma in situ	None	-	Well 5 years
7. M. W.	26	7 weeks	Squamous ca. of cx., Stage I	None	-	Well 3 years
8. M. G.	36	3 months (after tubal pregnancy)	Squamous ca. of cx., Stage I	None	-	Well 8 years
9. H. B.	49	6 months	Squamous ca. of cx., Stage II	X-ray	-	Well 5 years
10. M. T.	23	11 months	Squamous ca. of cx., Stage I	None	-	Well 3 years
11. M. C.	44	11 months	Adenocarcinoma of cx., Stage I	None	-	Died 7 months
12. F. L.	30	4 months (post abortion)	Squamous ca. of cx., Stage II	None	-	Well 2 years
13. E. H.	29	6 months	Squamous ca. of cx., Stage II	None	+	Well 1 year

node. A left ureterovaginal fistula then developed which healed spontaneously resulting in a functionless, symptomless left kidney. She is now an eleven-year cure. Her daughter is developing fairly normally, although her right forearm and leg are about an inch shorter than the left, and the right hand and foot are a little smaller than the left. The 2 cm. bald spot is still present in the left parietal region, although the remaining part of her scalp has abundant hair. Her intelligence seems adequate.

There were also 7 patients who were operated upon within one year of their last delivery. One of these is dead.

Sadugor and co-workers[3] made a comparison of the cure rate between pregnant and nonpregnant patients suffering from carcinoma of the cervix. The results in both groups were almost identical. In the present group of patients, pregnancy and recent parturition do not seem to be particularly deleterious in view of the fact that only one patient was lost in the entire group of thirteen and that this patient was 11 months post partum.

TABLE VI. PATIENTS WITH MULTIPLE CANCERS

1. A. M. 423059	a. Squamous carcinoma of cervix b. Scirrhous carcinoma of breast
2. C. H.	a. Squamous carcinoma of cervix b. Adenocarcinoma of breast
3. W. L. 567406	a. Squamous carcinoma of cervix b. Mucoid carcinoma of thyroid
4. M. M. 723	a. Squamous carcinoma of cervix b. Fibrosarcoma of abdominal wall
5. A. C. 20775	a. Squamous carcinoma of cervix b. Mucinous carcinoma simplex of stomach
6. M. F. 24270	a. Squamous carcinoma of cervix b. Carcinoma simplex of breast
7. A. K. 2444	a. Squamous carcinoma of cervix b. Carcinoma simplex of breast
8. A. B. 29878	a. Squamous carcinoma of cervix b. Adenocarcinoma of rectum
9. E. A. 21976	a. Squamous carcinoma of cervix b. Carcinoma simplex of breast
10. M. S. 677816	a. Squamous carcinoma of cervix b. Adenocarcinoma of endometrium
11. M. D. 536015	a. Squamous carcinoma of cervix b. Squamous carcinoma of nose
12. A. R. 21032	a. Squamous carcinoma of cervix b. Died of mucus-secreting tumor probably from bronchus, with metastasis to lung, pancreas, bladder, adrenals, liver, bone, and lymph node
13. C. C. 16187	a. Squamous carcinoma of cervical stump b. Adenocarcinoma of rectum
14. M. F. 472143	a. Adenocarcinoma of cervix b. Hemangiopericytoma of vulva
15. A. C. 50749	a. Adenocarcinoma of endometrium b. Colloid carcinoma of colon
16. E. J. 698028	a. Adenocarcinoma of endometrium b. Basal-cell epithelioma of nose
17. C. E. 15658	a. Adenocarcinoma of endometrium b. Carcinoid of appendix
18. I. S. 598783	a. Carcinoma in situ of cervix b. Squamous carcinoma of anterior thigh
19. R. S. 703254	a. Carcinoma in situ of cervix b. Adenocarcinoma in situ of uterine cervical glands
20. M. K. 578643	a. Carcinoma in situ of cervix b. Carcinoma in situ of vagina (with normal intervening tissue)
21. B. S. 574401	a. Squamous carcinoma of cervix b. Adenocarcinoma in situ of endometrium c. Carcinoid of appendix
22. E. B. 34320	a. Squamous carcinoma of cervix b. Carcinoma in situ of endometrium
23. B. M. 14436	a. Squamous carcinoma of cervix b. Adenocarcinoma of sigmoid
24. E. G. 440684	a. Squamous carcinoma of cervix b. Duct-cell carcinoma of breast

8. Multiple Cancers.—

Twenty-four patients in this series had more than one type of cancer, either in the genital tract or elsewhere in the body. The incidence of multiplicity of malignancy is 5 per cent. They are enumerated in Table VI. Warren and Gates[4] reported 1,078 cancer autopsies in which there was a 3.7 per cent double malignancy, and Slaughter[5] reported a 4 per cent incidence.

9. Family History of Cancer.—

A history of one or more members of the family who were known to have cancer was recorded in 89 of the 473 cases, an incidence of 19 per cent.

10. Castration Before Radical Surgery.—

Thirty-seven of the 473 patients were castrated 4 to 34 years previously, almost 8 per cent of the entire group. Bilateral oophorectomy had been employed in 28 cases and roentgen-ray castration in 9. Apparently oophorectomy does not protect an individual from the subsequent development of cancer in this region.

11. Adenomyosis and Endometriosis.—

Histologic examination of the surgical specimens removed in these 473 operations showed that 26 patients had had adenomyosis, and 34 patients had had endometriosis (Table VII). Of the 34 cases of endometriosis, 19 (56 per cent) were in the ovaries, 8 were in the paracervical region, 5 (15 per cent) in the regional nodes, 1 in the tube, and 1 in the vagina.

TABLE VII. INCIDENCE OF ADENOMYOSIS AND ENDOMETRIOSIS

Adenomyosis	26 (6%)
Endometriosis	34 (7%)
Ovary	19
Paracervical region	8
Lymph nodes	5
Fallopian tube	1
Vagina	1

12. The Ovarian Pathology.—

There were various pathologic changes noted in the ovaries of these patients, such as stromal hyperplasia, cortical granuloma, luteinization of stromal cells, hilus-cell rests, inclusion cysts, fibroma, and lymphangioma. Woll, Hertig, and Smith[6] reported that the ovaries of patients with carcinoma of the corpus were frequently found to have certain changes in the cortical stromal region not found in the ovaries of the control group of patients. In this present series, a comparison was made between the incidence of ovarian pathology in patients with carcinoma of the corpus and patients with squamous-cell carcinoma of the cervix. It was found the incidence of this previously mentioned ovarian pathology was lower in patients with carcinoma of the cervix. However, Brambell and Parkes[7] reported that the ovaries of mice exposed to x-rays were discovered to have stromal hyperplasia; and Furth and Butterworth[8] found that x-rays actually produced granulosa-cell tumors in the ovaries of mice. Among the 294 cases of squamous-cell carcinoma of the cervix in this series, 72, or 25 per cent, of the cases received preoperative irradiation, whereas among the 47 cases of carcinoma of the corpus, 22, or 47 per cent, of the cases received preoperative irradiation. The significance of these associated ovarian pathologies, in relation to carcinoma of the corpus is therefore, difficult to evaluate.

Metastasis to the ovaries from carcinoma of the corpus was found in 4 of the 47 patients, an incidence of 9 per cent. Finn[9] has reported a 13 per cent incidence of ovarian metastasis in 292 cases of carcinoma of the corpus.

13. Complications of Operation.—

One hundred twelve patients, or 24 per cent, had complications directly related to the operation. Pelvic hematoma and abscess formation occurred 15 times; thrombophlebitis requiring subsequent vein ligation occurred 8 times; and stricture of the ureter 7 times (2 of the patients with ureteral stricture required nephrectomy, one had nephrostomy, 2 had repeated dilatation of the ureter with subsequent good function, and 2 had functionless, symptomless kidneys as a result). The complications which occurred in the entire series are listed in Table VIII.

TABLE VIII. COMPLICATIONS OF 473 OPERATIONS

Urinary fistulas	45	(9%)
Pelvic hematoma and abscess	15	
Thrombophlebitis requiring vein ligation	8	
Stricture of ureter (not preceded by fistulas) (2 required nephrectomy)	7	
Urinary incontinence prolonged to 2 years	4	
Wound sepsis	4	
Pulmonary embolism	3	
Auricular fibrillation	3	
Ileus	3	
Rectal bleeding	2	
Intraperitoneal hemorrhage	2	
Intestinal obstruction	2	
Incisional hernia	2	
Dehiscence of wound	2	
Surgical shock	1	
Atelectasis	1	
Jaundice	1	
Pelvic peritonitis (immediately postoperative)	1	
Abdominal sinus	1	
Postoperative parotitis	1	
Exacerbation of rheumatic heart disease	1	
Failure of spinal anesthesia after 3 attempts	1	
Brachial palsy	1	
Subcutaneous emphysema of abdomen and chest	1	
Total	112	(24%)

14. Fistulas as a Complication of Operation.—

In 45 of the 473 patients operated upon, fistulas developed either in the urinary tract alone or in connection with the intestinal tract, a 9 per cent incidence. Fifteen (33 per cent) of these 45 patients had received preoperative irradiation (of the entire 473 cases, 139 patients, or 29 per cent, had received preoperative irradiation). The number of fistulas in relation to the number of operations each year, the types of diseases, and the types of fistulas are shown in Tables IX, X, and XI. Multiple fistulas occurred in 9 patients, all of whom received preoperative irradiation. Thomas and associates[10] reported 75 cases of radical hysterectomy. In 9, or 12 per cent, of their patients fistulas developed and 7 of these had received preoperative irradiation.

Morton[11] reported a 17 per cent incidence of fistulas among 119 operative cases of which 10 were vesicovaginal in type (2 healed), and 7 were definite and 3 were possible ureterovaginal in type (8 healed). In the present series of 45 fistulas, 15 healed spontaneously from one to ten months after the operation (Table XII). Of these, 13 were ureterovaginal and two were rectovaginal. Among the 13 patients with ureterovaginal fistulas that healed, 5

TABLE IX. 45 FISTULAS ACCORDING TO YEARS

YEAR	TOTAL NUMBER OF RADICAL HYSTERECTOMIES	NUMBER OF FISTULAS
1939	3	1
1940	12	1
1941	9	1
1942	19	1
1943	19	4
1944	19	2
1945	20	0
1946	24	2
1947	34	2
1948	57	6
1949	57	6
1950	54	3
1951	54	5
1952	55	7
1953	39	4

TABLE X. 45 FISTULAS ACCORDING TO THE DISEASE

DISEASE	TOTAL NUMBER	NUMBER OF FISTULAS
Squamous carcinoma of cervix	294	25
Adenocarcinoma of cervix	27	4
Stump carcinoma	23	2
Recurrent carcinoma of uterus	21	6
Carcinoma in situ	34	4
Carcinoma of corpus	47	3
Carcinoma of vagina	5	0
Leiomyosarcoma	1	0
Referred cases	21	1

TABLE XI. TYPES OF FISTULAS

a. Ureterovaginal	28	(Left 15, right 13)
b. Vesicovaginal	3	
c. Rectovaginal	3	
d. Vesicoureterovaginal	1	
e. Ureteroperitoneal	1	
f. Multiple	9	
Bilateral ureterovaginal		2
Vesicorectovaginal		2
Vesicovaginal and ureterovaginal		2
Left ureteroperitoneal and right ureterovaginal		1
Vesicovaginal and ileocutaneus		1
Rectovaginal and ileovaginal		1

had a resultant ureteral stricture (2 had subsequent hydronephrosis, one had nephrectomy, and 2 had preservation of renal function after reimplantation of the ureter in one case and repeated dilatation in the other); 5 had a nonfunctioning kidney; 2 had early recurrence; and one showed no impairment of renal function.

The outcome and the treatment of the patients with fistulas not spontaneously healed are shown in Table XIII. There were 17 cases of ureterovaginal fistulas not healed; in 5 the kidney was removed, nephrostomy was performed in 6, in 4 an anastomosis was made, and in 2 cases a simple ligation of the ureter was done.

15. Tumor Incompletely Removed at Operation.—

In 5 cases the tumor was incompletely removed from the pelvis and in 13 cases it extended to the excision edge of the vaginal cuff. Tables XIV and XV show the pathological report, additional treatment, and the outcome of

these 17 patients. Of the 5 patients whose tumor was incompletely removed from the pelvis, 4 are now dead and one has been well for five years. Among the 13 patients whose tumor was incompletely excised at the vaginal cuff, 8 had subsequent vaginectomy. Of these 8 patients, 6 have been alive and well from two to four years after the operation, the remaining 2 have recurrence now. Of the 5 patients who received no additional treatment, 3 are now dead and 2 are alive and well two and three years after the operation, respectively.

16. Preoperative Radiation.—

One hundred thirty-nine of the 473 patients (29 per cent) had received preoperative irradiation either (a) as the initial treatment of choice; (b) as a preliminary treatment to surgery in order to reduce the size and inflammation of the tumor; or (c) as a form of combined treatment. There were 72 cases of squamous-cell carcinoma of the cervix, 5 cases of adenocarcinoma of the cervix, 8 cases of carcinoma of the cervical stump, 13 cases of recurrent or residual carcinoma of the uterus, 22 cases of carcinoma of the corpus, one case of leiomyosarcoma of the cervix, one of carcinoma of the vagina, two of carcinoma in situ of the cervix, and 15 referred cases that had received preoperative radium, x-rays, or both in various doses.

TABLE XII. PATIENTS WITH FISTULAS SPONTANEOUSLY HEALED

PATIENT	YEAR	TYPE OF FISTULA	HEALED	OUTCOME
1. L. P.	1940	Ureterovaginal	2 months	Ureteral stricture in spite of repeated dilatation. Nephrectomy 9 months postoperatively. Well 12 years
2. A. A.	1943	Ureterovaginal	2 months	Nonfunctioning atrophic kidney. Died of pelvic recurrence 3 years after operation
3. H. H.	1943	Ureterovaginal	10 months	Nonfunctioning symptomless kidney. Alive and well 9 years
4. M. H.	1943	Ureterovaginal	1 month	Nonfunctioning symptomless kidney. Alive and well 9 years
5. E. G.	1943	Ureterovaginal	1 month	Nonfunctioning symptomless kidney. Alive and well 9 years
6. M. M.	1946	Ureterovaginal	6 weeks	Nonfunctioning kidney. Nephrostomy 1 month later. Died of metastasis 1 year after operation
7. L. T.	1946	Ureterovaginal	8 months	Early recurrence and metastasis. Died 1½ years after operation.
8. V. P.	1947	Ureterovaginal	1 month	Ureteral stricture and repeated dilatation. Well and normal renal function 5 years
9. P. P.	1948	Ureterovaginal	5 months	Ureteral stricture with hydronephrosis. Died of recurrence and metastasis 3½ years
10. V. F.	1949	Ureterovaginal	6 months	Ureteral stricture with hydronephrosis. Died of recurrence 1½ years
11. V. A.	1949	Ureterovaginal	3 months	Ureteral stricture with hydronephrosis. Reimplantation of ureters 4 months after operation. Well and normal renal function 3 years
12. J. R.	1953	Ureterovaginal	8 months	Recurrence
13. R. P.	1953	Ureterovaginal	6 months	No impairment of renal function
14. Y. T.	1951	Rectovaginal	6 months	No stricture. Well
15. E. G.	1953	Rectovaginal	2 months	No stricture. Well

The frequency of metastasis to the regional lymph nodes in the irradiated and nonirradiated cases in this study, exclusive of the referred and carcinoma in situ cases, is indicated in Table XVI along with the incidence in other series.[10, 12-15] In the present study lymph node metastasis was found in 28 per cent of the irradiated group and in 24 per cent of those nonirradiated.

TABLE XIII. PATIENTS WITH FISTULAS NOT SPONTANEOUSLY HEALED

PATIENT	YEAR	TYPE OF FISTULA	TREATMENT	OUTCOME
1. E. S.	1941	Ureterovaginal	Nephrostomy 2 months postoperatively. Distal ureter occluded. Ligation of ureter 3 months postoperatively	Died of recurrence 1 year
2. M. M.	1942	Ureterovaginal	Nephrostomy 1 month postoperatively. Nephrectomy 2 months postoperatively	Well 10 years
3. C. D.	1948	Ureterovaginal	Nephrectomy 5 months postoperatively	Well 4 years
4. F. S.	1948	Ureterovaginal	Nephrectomy 4 months postoperatively	Well 4 years
5. M. C.	1949	Ureterovaginal	Nephrectomy 1 month postoperatively	Died of recurrence 7 months
6. E. Y.	1949	Ureterovaginal	Nephrostomy 4 months postoperatively	Died of recurrence 6 months
7. A. W.	1949	Ureterovaginal	Nephrostomy 8 months postoperatively	Well 3 years
8. E. C.	1950	Ureterovaginal	Nephrostomy 1½ years postoperatively	Well 2 years
9. R. D.	1950	Ureterovaginal	Ligation of ureter 8 months postoperatively	Well 2 years
10. M. T.	1951	Ureterovaginal	Reimplantation of ureter 5 months postoperatively	Well 1 year
11. E. J.	1951	Ureterovaginal	Reimplantation of ureter 4 months postoperatively	Well 1 year
12. I. S.	1951	Ureterovaginal	Nephrectomy 5 months postoperatively	Well 2 years
13. H. O.	1952	Ureterovaginal	Reimplantation of ureter 3 months postoperatively	Well 1 year
14. A. F.	1952	Ureterovaginal	Nephrectomy 2 months postoperatively	Well 1 year
15. F. B.	1953	Ureterovaginal	Nephrostomy 1 month postoperatively	Well
16. C. E.	1940	Ureterovaginal, bilateral	Bilateral nephrostomy 4 months and 1 year postoperatively	Died of uremia 5 years
17. M. M.	1948	Ureterovaginal, bilateral	Reimplantation of ureter 2 months postoperatively	Died 2 years
18. H. F.	1939	Vesicovaginal	None	Died of recurrence 6 months
19. E. H.	1949	Vesicovaginal	Repair one year postoperatively	Well 4 years
20. M. S.	1952	Vesicovaginal	Repair 4 months potsoperatively	Well
21. B. L.	1950	Rectovaginal	Sigmoid colostomy 1 month postoperatively	Died of peritonitis postoperatively
22. M. H.	1944	Vesicoureterovaginal	Repair 7 months postoperatively	Well 8 years
23. M. S.	1949	Ureteroperitoneal	None	Died of uremia 11 months
24. C. A.	1951	Vesicorectovaginal	Transverse colostomy 1 month postoperatively	Died of uremia 8 months
25. M. L.	1952	Vesicorectovaginal	Transverse colostomy 2 weeks postoperatively	Urine draining slightly per vaginam
26. M. M.	1948	Vesicovaginal. Ileocutaneous	None	Died of peritonitis 3 months
27. E. B.	1947	Rectovaginal. Ileovaginal	None	Died of recurrence 1½ years
28. D. M.	1952	Right ureterovaginal, left ureteroperitoneal	Reimplantation of right ureter 1 month postoperatively, right nephrostomy, right ureterointestinal anastomosis. Left nephrostomy	Recurrence in left pelvis
29. M. T.	1952	Vesicovaginal. Left ureterovaginal	Repair of vesicovaginal fistula 3 months postoperatively, second repair 4 months later. Reimplantation of left ureter 3 months postoperatively	Well
30. L. C.	1953	Vesicovaginal. Left ureteroperitoneal	None	Primary mortality

TABLE XIV. PATIENTS WITH TUMOR INCOMPLETELY REMOVED FROM PELVIS

PATIENT	PATHOLOGICAL REPORT	ADDITIONAL TREATMENT	OUTCOME
A. D. 666937	1. Squamous carcinoma of cervix with metastasis to paracervical lymphatics and nodes of right iliac and obturator 2. Gross tumor left behind	X-ray	Died 1½ years
E. R. 633843	1. Squamous carcinoma of cervix extended to vagina and lymphatics 2. Metastasis to obturator node 3. Tumor infiltrated cervical wall and noted to be grossly within 0.5 cm. of cul-de-sac	None	Well 5 years
E. P. 746770	1. Adenocarcinoma of cervix 2. Extensive involvement of cervical and paracervical tissue 3. Metastasis to obturator and vaginal nodes 4. Tumor seemed to have been incompletely excised in the paracervical region	X-ray	Died 1½ years
L. D. 25969	1. Squamous carcinoma of cervix 2. Uterus hourglass shape, cervix larger than corpus 3. Disease extended to broad ligament, incompletely excised	X-ray	Died 1½ years
E. F. 23461	1. Adenoacanthoma of vagina of questionable endocervical origin 2. Metastasis to vagina and broad ligament apparently incompletely excised	None	Died three days postoperatively of atelectasis and ileus

TABLE XV. PATIENTS WITH TUMOR INCOMPLETELY REMOVED FROM VAGINAL CUFF

PATIENT	YEAR	PRIMARY DISEASE	ADDITIONAL TREATMENT	FINDINGS IN SPECIMEN	OUTCOME
J. C.	1949	Squamous carcinoma of cervix, Stage II	Vaginectomy 5 months postoperatively	Invasive carcinoma	Well 4 years
W. K.	1950	Squamous carcinoma of cervix, Stage II	None		Dead
E. W.	1950	Squamous carcinoma of cervix, recurrent in vagina	None		Well 3 years
I. N.	1950	Adenocarcinoma of cervix, Stage II	None		Dead
E. W.	1950	Squamous carcinoma of cervix, Stage II	Vaginectomy 2 weeks postoperatively	Carcinoma in situ	Well 3 years
M. Z.	1950	Squamous carcinoma of cervix, Stage II	Vaginectomy 2 weeks postoperatively	Invasive carcinoma	Well 3 years
I. P.	1950	Squamous carcinoma of cervix, Stage I	Vaginectomy 2 months postoperatively	No carcinoma	Well 3 years
M. K.	1951	Squamous carcinoma of cervix, Stage II	Vaginectomy 6 weeks postoperatively	No carcinoma	Well 2 years
C. H.	1951	Squamous carcinoma of cervix, Stage I	None		Dead
J. R.	1952	Squamous carcinoma of cervix, Stage I	Vaginectomy 1 month postoperatively	No carcinoma	Recurrence
N. O.	1952	Squamous carcinoma of cervix, Stage I	Vaginectomy 2 weeks postoperatively	Carcinoma in situ	Well 1 year
M. H.	1952	Squamous carcinoma of cervix, Stage I	None		Well 2 years
A. D.	1953	Squamous carcinoma of cervix, Stage II	Vaginectomy 3 months postoperatively	Invasive carcinoma and carcinoma in situ	Recurrence

The interpretation of these figures is difficult because of the variable circumstances. Evidence of the effectiveness of radiation upon node metastasis has been lacking, although Morton[14] suggests that modern radiotherapy can and often does destroy cancer in regional lymph nodes.

Because the present series includes different types of disease, the dosages of irradiation were not at all uniform; neither were the time intervals between irradiation and surgery equal, the figures given therefore serve to show only the general picture of this particular group.

Among the 139 patients, however, who received preoperative irradiation (x-ray, radium, or both) from immediately preoperative to two or more years before the operation, the surgical specimen in 72 instances showed the effect of irradiation. Of these, residual viable cancer cells were present in 43 cases and no viable malignant cells in the remaining 29 (Table XVII).

In this small group of 72 patients who had received preoperative irradiation and showed radiation changes in the local tissue, 19, or 26 per cent, had lymph node metastasis.

TABLE XVI. INCIDENCE OF LYMPH NODE METASTASIS IN IRRADIATED AND NONIRRADIATED GROUPS

SERIES	OPERATION	PREOPERATIVE IRRADIATION			NO PREOPERATIVE IRRADIATION			TOTAL		
		NUMBER OF PATIENTS	POSITIVE NODES		NUMBER OF PATIENTS	POSITIVE NODES		NUMBER OF PATIENTS	POSITIVE NODES	
			NO.	%		NO.	%		NO.	%
1. Taussig 1943	Lymphadenectomy	175	47	27				175	47	27
2. Meigs 1945	Wertheim	24	5	21	41	7	17	65	12	18
3. Thomas et al. 1948	Wertheim	42	9	21	33	8	24	75	17	23
4. Morton 1950	Lymphadenectomy	43	7	16	60	18	30	103	25	24
5. Gorton 1953	and Wertheim	181	28	16				181	28	16
6. Present series	Lymphadenectomy	122	34	28	296	70	24	418	104	25
Total surgical series*	Wertheim	563	125	22	389	98	25	952	221	23

*Meigs' 1945 series is not added in the total because it is included in the present series.

TABLE XVII. IRRADIATED CASES SHOWING RADIATION EFFECT

	RADIATION EFFECT WITH VIABLE CANCER (43 CASES)	RADIATION EFFECT WITHOUT VIABLE CANCER (29 CASES)
Positive nodes	11	8
Negative nodes	32	21

17. Lymph Node Metastasis.—

Out of 418 patients with invasive cancer (the carcinoma in situ and referred cases were excluded), lymph node metastasis was found at operation in 104 cases, or 25 per cent. It was found in 74 of 294 cases of squamous-cell carcinoma of the cervix; 10 of the 27 cases of adenocarcinoma of the cervix; 4 of the 23 cases of carcinoma of the cervical stump; 11 of the 47 cases of

carcinoma of the corpus; 4 of the 21 cases of recurrent or residual carcinoma of the uterus, and one of the 4 cases of carcinoma of the vagina (Table XVIII).

Among the lymph nodes with metastasis, as shown in Table XIX, the obturator group is the one most frequently involved, which is in agreement with the findings of Leveuf,[16] Bonney,[17] and Gorton.[15] The aortic nodes were involved in 2 patients. One patient had squamous-cell carcinoma of the cervix, Stage I, with metastatic carcinoma found in eleven nodes as high up as the bifurcation of the aorta. She received postoperative deep x-ray and is well two years after the operation. Another patient had a squamous-cell carcinoma of the cervix, Stage II (vagina), with metastatic carcinoma found in four nodes including the aortic. She received preoperative and postoperative irradiation and is well two years after the operation. When metastasis was present, often more than one node was involved. The largest number of metastatic lymph nodes removed from one patient was sixteen.

TABLE XVIII. TOTAL INCIDENCE OF LYMPH NODE METASTASIS

TUMORS	NO. OF CASES	POSITIVE NODES	
		NO.	%
Squamous carcinoma of cervix	294	74	25
Adenocarcinoma of cervix	27	10	37
Carcinoma of cervical stump	23	4	17
Recurrent or residual carcinoma of uterus	21	4	19
Leiomyosarcoma of cervix	1	0	
Carcinoma of corpus	47	11	23
Carcinoma of vagina	5	1	20
Total	418	104	25

TABLE XIX. POSITION OF POSITIVE LYMPH NODES IN 104 CASES

NODES	NUMBER OF TIMES INVOLVED
Obturator	52
Common iliac	49
External iliac	21
Perivaginal	9
Pericervical	9
Parametrial	4
Hypogastric	4
Aortic	2
Presacral	2
Ovarian	1
Paravesical	1
Ureteral	1

TABLE XX. LYMPH NODE METASTASIS IN REGARD TO ANATOMICAL LOCATION OF CARCINOMA OF CORPUS

	NO. OF CASES	LYMPH NODES POSITIVE	LYMPH NODES NEGATIVE
Carcinoma confined to corpus	33	4 (12%)	29
Carcinoma involved corpus and cervix	14	7 (50%)	7
Total	47	11 (23%)	36

18. Lymph Node Metastasis and Carcinoma of the Corpus.—

It has been thought that when a corpus carcinoma also involves the cervix, it behaves differently than when the lesion is entirely confined to the corpus. Of the 47 cases of corpus carcinoma, 33 were confined to the corpus

TABLE XXI. LYMPH NODE METASTASIS IN REGARD TO MYOMETRIAL INVASION OF CARCINOMA OF CORPUS

	NO. OF CASES	LYMPH NODES POSITIVE	LYMPH NODES NEGATIVE
No myometrial invasion	25	1 (4%)	24
With myometrial invasion	22	10 (45%)	12
Total	47	11 (23%)	36

TABLE XXII. LYMPH NODE ANOMALIES

TUMOR	NODES	PREOPERATIVE RADIATION	NODE ANOMALIES	OUTCOME
Squamous ca. of cx., Stage I	-	0	Epithelioid anomaly with acini structure filled with pink homogeneous material	Well 9 years
Squamous ca. of cx., Stage I	- Blood-vessel invasion	Yes	Epithelioid anomaly with granular mucinoid material	Dead
Squamous ca. of cx., Stage I	+	0	Sarcoid reaction in lymph nodes	Dead
Squamous ca. of cx., Stage I	-	Yes	Sarcoid reaction in lymph nodes	Well 6 years
Squamous ca. of cx., Stage I	-	0	One node has epithelioid anomaly	Well 8 years
Squamous ca. of cx., Stage I	-	0	Small foci of tuberculosis	Dead
Squamous ca. of cx., Stage I	-	Yes	Obsolete tuberculosis in two nodes	Well 7 years
Squamous ca. of cx., Stage I	- Lymph vessel invasion	Yes	Hyperplastic lymph nodes	Recurrence
Squamous ca. of cx., Stage I	-	0	Hyperplastic lymph nodes	Dead
Squamous ca. of cx., Stage I	-	0	Hyperplastic lymph nodes	Well 10 years
Squamous ca. of cx., Stage I	-	0	Lymphadenitis	Dead
Squamous ca. of cx., Stage II	+	Yes	Reticulum-cell hyperplasia with large pink polyhedral cells and bland nuclei	Dead
Carcinoma of cervical stump	-	Yes	Radiation reaction in nodes	Well 8 years
Recurrent carcinoma	-	Yes	Radiation reaction in nodes	Well 11 years
Carcinoma in situ and pregnancy	-	0	Chronic lymphadenitis	Well 3½ years
Carcinoma of endometrium	-	0	Chronic lymphadenitis	Well 2 years
Referred case	-	Yes	Cervical node contains granuloma	
Referred case	-	Yes	Parametrial node has tuberculosis	

and 14 involved the cervix. Table XX shows that, of the 33 patients in whom the lesion was confined to the corpus, only 4 (12 per cent) had lymph node metastasis; but of the 14 whose lesions involved both corpus and cervix, 7 (50 per cent) showed lymph node metastasis.

The incidence of lymph node metastasis in 47 patients with carcinoma of the corpus is again analyzed in relation to cancerous invasion of the underlying myometrium. It was found that in 22 patients whose corpus carcinoma involved the myometrium, 10, or 45 per cent, had lymph node metastasis; but in 25 patients whose lesions were limited to the endometrium, only 1, or 4 per cent, had lymph node metastasis (Table XXI).

19. Lymph Node Anomalies.—

There were 18 patients in this series who had microscopic anomalies in the lymph nodes other than metastatic carcinoma and endometriosis. Nine of these had received preoperative irradiation.

In 3 cases the lymph nodes showed hyperplastic changes, in 3 tuberculosis, in 1 granuloma, in 4 they were described as having epithelioid anomalies, in 2 sarcoid changes, in 3 chronic lymphadenitis, and in 2 radiation reaction (Table XXII). Nadel and Ackerman[18] described sarcoidlike lesions in lymph nodes draining an area containing a malignant neoplasm. Gorton[15] also reported 10 cases with epithelioid changes in nodes that contained no tumor. The significance of these findings is undetermined.

20. Primary Mortality.—

Eight patients died after the operation before leaving the hospital, a 1.7 per cent surgical mortality. Two of these patients died of massive pulmonary embolism, 2 died of peritonitis, 2 died of shock and its sequelae, 1 died of sepsis and ileus, and 1 of a ruptured aneurysm of the circle of Willis (Table XXIII). The age of these patients ranged from 51 to 76 years of age.

TABLE XXIII. PRIMARY MORTALITY

PATIENT	YEAR	AGE	DIAGNOSIS	DAY OF DEATH	CAUSE OF DEATH
E. F.	1948	67	Recurrent adenocarcinoma of corpus	Third postoperative day	Shock, atelectasis, and ileus (autopsy)
E. C.	1948	51	Recurrent adenocarcinoma of corpus	Sixth postoperative day	Pulmonary embolism (autopsy)
M. W.	1949	68	Adenocarcinoma of corpus	Fifth postoperative day	Massive pulmonary emboli extending from left ventricle (autopsy)
N. M.	1950	76	Adenocarcinoma of corpus	Seventh postoperative day	Peritonitis
C. L.	1950	56	Squamous carcinoma of vagina	Seventh postoperative day	Ruptured aneurysm of circle of Willis with massive subarachnoid and intracranial hemorrhage (autopsy)
B. L.	1950	57	Squamous carcinoma of cervix, Stage III	Developed rectovaginal fistula. A colostomy was done. Died on twentieth postoperative day	Peritonitis (autopsy)
F. W.	1952	59	Adenocarcinoma of corpus	Third postoperative day	Shock and renal failure (autopsy)
L. C.	1953	60	Adenoacanthoma of corpus	Twenty-seventh postoperative day	Sepsis and ileus (autopsy)

TABLE XXIV. SUMMARY OF CLINICAL COURSE OF 71 PATIENTS WHO DIED

PATIENTS		RECURRENCE		METASTASES		CLINICAL COURSE	DIED
		VAGINAL	PELVIC	BONY	SOFT TISSUE		
Squamous-Cell Carcinoma of Cervix—51 Cases.—							
1. K. D.	14311		+				3 years
2. M. R.	662978	+					2 years
3. J. T.	617213		+	Ribs, pelvis			1 year
4. V. D.	681653		+				1½ years
5. C. B.	381883	+	+			Rectovaginal and ileovaginal fistulas	1½ years
6. W. K.	434343					Incomplete removal of tumor at vaginal cuff	1½ years
7. E. A.	251767		+			Intestinal and urinary obstruction	4 years
8. E. D.	35522		+				4 months
9. L. B.	213542	+	+			Urinary obstruction	1½ years
10. F. V.	603740						4½ years, heart disease
11. E. J.	124281		+			Urinary obstruction	8 months
12. P. Y.	603102		+			Urinary obstruction	8 months
13. A. R.	125052						4 months
14. C. H.	731223	+	+			Urinary obstruction, cerebral hemorrhage; tumor was incompletely removed from vaginal cuff	9 months
15. I. C.	15890	+	+			Hemorrhage	1½ years
16. V. F.	683186	+	+			Ureterovaginal fistula, healed	1½ years
17. E. Y.	27917	+	+	Femur		Ureterovaginal fistula and nephrostomy. Urinary obstruction and massive hemorrhage	6 months

18. E. S.	18645	+	+	Femur		Ureterovaginal fistula, urinary obstruction	1 year
19. A. A.	428999		+			Ureterovaginal fistula, healed. Intestinal obstruction	3 years
20. G. A.	558654		+			Intestinal obstruction	2½ years
21. S. K.	581147		+		Lung, pericardium		3 years
22. E. M.	547964		+			Urinary obstruction	1 year
23. M. D.	583439	+	+			Radiation colitis, urinary obstruction	2 years
24. S. S.	749584	+	+			Rectal bleeding	1½ years
25. A. D.	666937		+		Lung	Tumor was incompletely removed from pelvis	1½ years
26. I. W.	25600						4½ years, bronchopneumonia
27. L. D.	25969	+	+			Intestinal obstruction. Tumor was incompletely removed from pelvis	1½ years
28. E. R.	16074				Lung	Pulmonary insufficiency	2 years
29. F. W.	496156		+			Urinary obstruction	2 years
30. C. G.	15694	+	+	Pubic arch		Anterior exenteration. Multiple seeds in perineum with rectal stricture	3½ years
31. H. D.	425174		+				2 years
32. E. W.	18779						4½ years, heart disease
33. M. M.	2295		+		Supraclavicular node and mediastinum		3½ years
34. Y. F.	441482						2 years
35. B. C.	679599		+			Intestinal obstruction	2½ years
36. H. T.	22332	+	+		Supraclavicular node and lung	Pulmonary insufficiency and hemoptysis	1½ years

PATIENTS	RECURRENCE		METASTASES		CLINICAL COURSE	DIED
	VAGINAL	PELVIC	BONY	SOFT TISSUE		
37. M. W. 24320						4½ years
38. A. M. 423159						7 years, heart disease
39. M. F. 24270						7 years, breast cancer
40. C. C. 21504	+	+			Intestinal obstruction	1½ years
41. A. C. 699437	+	+		Lung	Urinary obstruction	2½ years
42. E. S. 653032				Miliary metastasis to upper abdomen	Intestinal obstruction	2½ years
43. M. A. 789071		+			Urinary obstruction	4 months
44. A. S. 762580	+	+			Intestinal obstruction	2 years
45. M. L. 753076	+	+			Intestinal obstruction	1 year
46. M. S. 677816		+			Ureteroperitoneal fistula	1 year
47. L. T. 540067		+	Spine		Ureterovaginal fistula	2 years
48. L. G. 24974	+	+			Intestinal obstruction	2 months
49. E. H. 13776		+			Urinary obstruction	5 months
50. M. W. 594411					Psychosis, barbiturate poisoning	1 year, suicide
51. J. W. 649911					Advanced pulmonary tuberculosis. Died in sanatorium	4½ years, tuberculosis
Adenocarcinoma of Cervix—10 Cases.—						
1. W. B. 696286		+			Intestinal obstruction, urinary obstruction	7 months
2. E. N. 323011	+	+			Urinary obstruction	1½ years
3. E. P. 746770		+			Tumor was incompletely excised in the paracervical region	1½ years

4. Z. B.	347360	+	+			Urinary obstruction	2 years
5. C. M.	659365	+	+			Intestinal obstruction. Total exenteration	2½ years
6. P. P.	615238		+		Supraclavicular node and brain	Ureterovaginal fistula healed	3½ years
7. C. C.	17948		+			Bilateral ureterovaginal fistulas, bilateral nephrostomy. Urinary obstruction	6 years
8. L. R.	20931	+	+		Supraclavicular node	Intestinal obstruction	6 years
9. H. P.	16897		+			Urinary obstruction	6 years
10. C. W.	481145		+		Lung	Urinary obstruction	6 years
Carcinoma of Cervical Stump—4 Cases.—							
1. A. M.	448932	+	+			Psoas abscess	3 years
2. C. A.	144398					Vesicorectovaginal fistula, colostomy, and uremia	8 months
3. A. P.	663009		+	Spine	Supraclavicular node	Hemorrhage	2½ years
4. L. S.	791127					Died at home	8 months
Carcinoma of Corpus—6 Cases.—							
1. S. A.	597707	+			Lung		1 year
2. R. M.	789113	+	+			Intestinal obstruction, colostomy	13 months
3. N. S.	668882	+			Lung	Pulmonary insufficiency	2½ years
4. E. S.	605616		+		Lung		2½ years
5. L. J.	621456				Lung	Pulmonary insufficiency, intestinal obstruction	3½ years
6. M. M.	620875		+		Lung, esophagus	Left ureterovaginal fistula healed. Right Ureteral stricture, nephrostomy	1 year

21. Deaths and Causes of Death.—

In all, 100 patients in the series are now dead. One-third of the deaths occurred in the first year following the operation, and 85 per cent of the patients who could not survive five years died in three and one-half years postoperatively.

Autopsy was performed in 28 cases (28 per cent). Seven of the 28 cases were in the primary mortality group. The findings in the remaining 21 cases are abstracted below:

A. C., No. 20775. Squamous-cell carcinoma of cervix, Stage I, Grade II, with invasion of lymphatic channels. Signs of pyloric obstruction developed, and the patient died two and one-half years after the operation.

Autopsy: Mucinous carcinoma simplex of stomach, infiltrating and extending to peritoneum, diaphragm, and omentum; adenocarcinoma metastasized to lesser and greater curvature, lungs, and spleen; perforation of stomach with localized peritonitis; no signs of pelvic recurrence.

D. A., No. 25805. Squamous-cell carcinoma of cervix, Stage I, Grade II. Developed nonproductive cough and died of pulmonary insufficiency 15 months after the operation.

Autopsy: Squamous carcinoma metastasized to lungs with extension to thoracic wall.

I. R., No. 24210. Squamous-cell carcinoma of cervix, Stage I, Grade III. Developed signs of cardiac failure and massive pleural effusion and died five months after the operation.

Autopsy: Squamous carcinoma involving mediastinum and both lungs; obstruction of superior vena cava.

A. R., No. 21032. Squamous-cell carcinoma of cervix, Stage I, Grade III. No signs of pelvic or vaginal recurrence until two years after operation except weight loss and general body aching. Died after two and one-half years at home.

Autopsy: Mucus-secreting carcinoma found in lungs, pancreas, gall bladder, adrenal, liver, vertebrae, and peritoneal lymph nodes. Site of origin of this tumor could not be determined with certainty but the suggested sites were pancreas and mucous glands of the bronchus; no pelvic disease.

M. S., No. 20177. Squamous carcinoma of cervix, Stage II (parametrium) with preoperative irradiation. The surgical specimen showed radiation reaction with foci of residual carcinoma in the cervix, broad ligament blood vessels, and iliac nodes. Died two and one-half years later of uremia and generalized peritoneal metastasis.

Autopsy: Squamous carcinoma, recurrent, with massive metastasis to liver, lung, vertebrae, pelvic tissue and along the course of the left sciatic nerve; large retroperitoneal mass of lymph nodes behind pylorus; conspicuous invasion of nerves, many nerves completely destroyed by the tumor.

W. L., No. 567406. Squamous-cell carcinoma of cervix, Stage I, Grade III, with preoperative irradiation and metastasis in the iliac node. Died two and one-half years after operation of cerebral metastasis without local recurrences.

Autopsy: Metastatic carcinoma to brain, thyroid, liver, kidney, and pancreas.

B. S., No. 639423. Squamous-cell carcinoma of cervix, Stage I, Grade II. Vaginal and pelvic recurrences one and one-half years after operation. Death from intestinal obstruction and renal obstruction two and one-half years after the operation.

Autopsy: Bilateral ureteral obstruction with hydroureter and hydronephrosis; squamous carcinoma metastasized to sigmoid, ileum; cardiac hypertrophy.

F. S., No. 734708. Squamous-cell carcinoma of cervix, Stage II (vagina), Grade IV, with metastasis to perivaginal lymph nodes. Death from intestinal obstruction three months after operation.

Autopsy: Squamous carcinoma metastasized to peritoneum, diaphragm, regional lymph nodes, bladder, intestines, liver, spleen, and lungs; intestinal obstruction due to tumor; bilateral pyelonephritis.

A. W., No. 422476. Squamous-cell carcinoma of cervix, Stage II (vagina), Grade III, with preoperative radiation and metastasis to obturator node. Pelvic and vaginal recurrences and patient died of hemorrhage eleven months after operation.

Autopsy: Squamous carcinoma involving bladder, ureter, vagina, rectum, pelvic and retroperitoneal lymph nodes; peritonitis; pulmonary edema and congestion; pleuritis.

M. H., No. 345032. Squamous-cell carcinoma of the cervix, Stage I, Grade III, with metastasis to ovarian, iliac and obturator nodes. Vaginal recurrence and supraclavicular lymph node metastasis. Died nine months after operation.

Autopsy: Squamous carcinoma extending to bladder, sigmoid, and iliac lymph node; metastasized to mediastinal and supraclavicular nodes; retroperitoneal abscesses.

H. S., No. 605361. Squamous-cell carcinoma of cervix, Stage II (vagina), Grade II, with metastasis to iliac lymph nodes. Pelvic recurrence nine months after operation. Three years after operation, died of intestinal perforation and peritonitis following x-ray therapy.

Autopsy: Fibrosis and ulceration of ileum; obstruction of rectum; peritonitis.

M. M., No. 723. Squamous-cell carcinoma of cervix, Stage II (vagina), Grade II, with preoperative irradiation and invasion of lymphatic channel. Developed vesicovaginal and abdominal intestinal fistula and died three months after operation.

Autopsy: Rectovesicovaginal fistula (radiation); radiation proctitis and ileitis; fibrinous peritonitis; bilateral pyelonephritis; no evidence of residual carcinoma in pelvis.

J. S., No. 731395. Squamous-cell carcinoma of cervix, Stage II (parametrium), Grade II. Developed severe right hydronephrosis with pelvic sepsis. Right nephrectomy one month after operation. Died of uremia 14 months after operation.

Autopsy: Marked hydronephrosis of left kidney with blocking of ureter near bladder from scar tissue; no recurrence of pelvic disease.

H. C., No. 621632. Squamous-cell carcinoma of cervix, Stage II (parametrium), Grade III, with metastasis to obturator and common iliac nodes. Pelvic recurrence, bilateral urinary obstruction and nephrostomy four months after operation. Died 13 months after operation.

Autopsy: Recurrent carcinoma involving the entire pelvis and retroperitoneal lymph nodes; pelvic abscess with fistula to abdominal wall; bilateral pyoureter; acute splenitis.

H. F., No. 4462. Squamous-cell carcinoma of cervix, Stage I, Grade II, with preoperative irradiation. Surgical specimen showed radiation reaction with residual carcinoma. Developed vesicovaginal fistula and pelvic abscess. Died of pelvic recurrence and sepsis six months after operation.

Autopsy: Residual carcinoma in pelvis, including colon and bladder, aortic and inguinal lymph nodes.

M. C., No. 27629. Adenocarcinoma of cervix, Stage II, with metastasis to obturator node. Developed left ureterovaginal fistula with multiple renal abscesses. Left nephrectomy one month after operation. Rapid development of pelvic and vaginal recurrences. Developed uremia and died of pulmonary edema and heart failure after an intravenous injection of glucose.

Autopsy: Adenocarcinoma at vaginal apex, extending to pelvic wall, rectum, bladder, and ureter; metastasized to common iliac nodes, lungs, and adrenals; right hydroureter and hydronephrosis; cardiac hypertrophy; bilateral atelectasis and pleural effusion.

I. J., No. 622259. Adenocarcinoma of cervix, Stage I, with metastasis to iliac nodes. Pelvic recurrence two months after operation, with intestinal obstruction and urinary obstruction for which ureterostomy was done. Death due to cerebral accident three months after operation.

Autopsy: Extensive subarachnoid hemorrhage, probably from ruptured aneurysm of right cerebral artery; bronchial pneumonia; bilateral ureteral obstruction and pyelonephritis; uncertain residual carcinoma in pelvis.

E. D., No. 792189. Adenocarcinoma of cervix, Stage I. One year later vaginal recurrence was detected and radium was given. Metastasis to supraclavicular node. Died of pulmonary metastasis five months after the operation.

Autopsy: Adenocarcinoma of cervix with metastasis to lungs, peritoneum, and liver; massive pulmonary embolism; phlebothrombosis, common iliac and external iliac; ascites and pleural effusions.

F. B., No. 27468. Adenocarcinoma of corpus with preoperative irradiation. Died one month after operation.

Autopsy: Pyelonephritis with abscess and thrombosis; purulent cystitis; thrombosis of iliac vein and aorta; bronchopneumonia.

B. W., No. 16421. Adenocarcinoma of corpus with metastasis to iliac node and ovary. Pelvic recurrence one and one-half years after operation with urinary obstruction and uremia. Pelvic exenteration done. Died of generalized carcinomatosis five months after exenteration.

Autopsy: Intrapelvic and abdominal metastatic carcinoma involving parietal and visceral peritoneum and lymph nodes; hydroureter and nonfunctioning left kidney.

L. P., No. 633836. Adenocarcinoma of the corpus with preoperative radiation and metastasis to myometrium and lymph nodes. Diabetes not controlled after operation; wound sepsis. Death two months after operation, due to congestive heart failure.

Autopsy: Recurrent carcinoma of endometrium, metastasized to urethra, lung, pleura, pericardium, paratracheal, paraesophageal, and abdominal nodes; bilateral hemorrhagic hydrothorax; bilateral atelectasis.

A survey was also made of the remaining 71 cases in which necropsy was not performed in order to ascertain the contributing causes of death as observed clinically (Table XXIV). Ward and co-workers[19] analyzed the causes of death in 248 cases of cervical carcinoma and reported that 65 per cent of the deaths were due to urinary obstruction and hemorrhage. In the present series of 100 deaths, 84 were in patients with carcinoma of the cervix. Of these, urinary obstruction in the terminal stage with or without frank symptoms of uremia appeared 27 times in the 84 records, intestinal obstruction 17 times, vaginal or rectal hemorrhage 5 times, and pelvic sepsis 6 times. Seven of the 84 patients who died with carcinoma of the cervix had bony metastasis; 14 had lung metastasis; 7 had metastasis to supraclavicular nodes; 4 had metastasis to the mediastinum; and 3 had brain metastasis.

PART II. RADICAL HYSTERECTOMY AND CARCINOMA OF THE CERVIX.

1. Squamous Carcinoma of the Cervix.—

A total of 294 cases of invasive squamous-cell carcinoma of the cervix were treated with radical hysterectomy and pelvic lymphadenectomy. There were 193 cases in Stage I; 99 in Stage II, and 2 cases in Stage III. Seventy-two of these 294 cases were treated with preoperative irradiation. The involvement of lymph nodes in regard to clinical stages and preoperative irradiation are shown in Table XXV.

It is seen that 222 patients with squamous-cell carcinoma of the cervix did not receive any form of preoperative irradiation; the radical operation was the primary treatment of their disease. In this uncomplicated group, 152 were Stage I patients, 26 (17 per cent) of whom had positive nodes, and 69 were Stage II, 28 (40 per cent) of whom had positive lymph nodes.

TABLE XXV. 294 CASES OF SQUAMOUS CARCINOMA OF CERVIX

STAGE	NO. OF CASES	PREOPERATIVE IRRADIATION LYMPH NODES		NO PREOPERATIVE IRRADIATION LYMPH NODES		TOTAL LYMPH NODES	
		POSITIVE	NEGATIVE	POSITIVE	NEGATIVE	POSITIVE	NEGATIVE
Stage I	193	8	33	26 (17%)	126	34 (18%)	159
Stage II	99	11	19	28 (40%)	41	39 (40%)	60
Stage III	2	0	1	1	0	1	1
Total	294	19	53	55	167	74 (25%)	220

Between February, 1939, and June, 1949, 165 patients who had invasive squamous-cell carcinoma of the cervix were treated surgically. Among the 165 patients, 63 received preoperative irradiation. One hundred sixteen patients of the 165 had Stage I cases, and 49 had Stage II. The survival rate of Stage I patients is 74 per cent, and that of Stage II, 57 per cent (Table XXVI).

TABLE XXVI. FIVE-YEAR RESULT OF 165 CASES OF SQUAMOUS CARCINOMA OF CERVIX (IN REGARD TO CLINICAL STAGES)

Stage I	116 cases	
	*86 alive and well	(74%)
	†30 dead	(26%)
Stage II	49 cases	
	‡28 alive and well	(57%)
	§21 dead or with recurrence	(43%)

*Four patients developed vaginal recurrences who were subsequently irradiated and are alive and well. Two patients died of breast cancer 7 years postoperatively without clinical recurrence.

†Five patients died of intercurrent diseases without clinical recurrence.

‡Two patients had vaginal recurrences who had subsequent total vaginectomy and are alive and well now. One patient received postoperative irradiation shortly after the operation.

§One patient has metastasis to spine and one patient developed pelvic and vaginal recurrence who had pelvic exenteration 7 months after the radical hysterectomy and now has recurrence.

Since the evaluation of the clinical extent of the disease varies with personal interpretation of the palpatory findings, especially in the presence of inflammation and edema, and since involvement of lymph nodes yields significant criteria on which to base prognosis, it might be helpful to examine the data of these 165 patients in regard to their lymph node involvement. When the patients in Stage I and Stage II are combined, it is found that 122

had negative lymph nodes and 43 had positive lymph nodes. Of the group with the negative lymph nodes, the survival rate is 82 per cent, of the group with positive lymph nodes, 33 per cent survived (Table XXVII).

TABLE XXVII. FIVE-YEAR RESULT OF 165 CASES OF SQUAMOUS CARCINOMA OF CERVIX (IN REGARD TO LYMPH NODE METASTASIS)

STAGE I 116 CASES		STAGE II 49 CASES		STAGES I AND II COMBINED 165 CASES	
Nodes negative 95		Nodes negative 27		Nodes negative 122	
*78 alive and well	(82%)	22 alive and well	(85%)	*100 alive and well	(82%)
†17 dead		5 dead		† 22 dead	
Nodes positive 21		Nodes positive 22		Nodes positive 43	
8 alive and well	(38%)	‡ 6 alive and well	(27%)	‡ 14 alive and well	(33%)
13 dead		§16 dead or with recurrence		§ 29 dead or with recurrence	

*Four patients developed vaginal recurrences who were subsequently irradiated and are alive and well. Two patients died of breast cancer 7 years postoperatively without clinical recurrence.

†Five patients died of intercurrent diseases without clinical recurrence.

‡Two patients had vaginal recurrences who had subsequent total vaginectomy and are alive and well now. One patient received postoperative irradiation shortly after the operation.

§One patient has metastasis to spine and one patient developed pelvic and vaginal recurrence who had pelvic exenteration 7 months after the radical hysterectomy and is now having recurrence.

2. Adenocarcinoma of the Cervix.—

There were 27 cases of adenocarcinoma of the cervix treated with radical hysterectomy and pelvic lymphadenectomy. Of these 27 cases, 22 were considered to be Stage I and 5 were Stage II. In 5 cases preoperative irradiation was given. The involvement of lymph nodes at the time of operation is shown in Table XXVIII.

There were 15 patients with adenocarcinoma of the cervix who were treated before June, 1949; 8 of these survived five or more years (Table XXIX).

TABLE XXVIII. 27 CASES OF ADENOCARCINOMA OF CERVIX

STAGE	NO. OF CASES	PREOPERATIVE IRRADIATION		NO PREOPERATIVE IRRADIATION		TOTAL	
		LYMPH NODES		LYMPH NODES		LYMPH NODES	
		POSITIVE	NEGATIVE	POSITIVE	NEGATIVE	POSITIVE	NEGATIVE
Stage I	22	1	3	4	14	5 (23%)	17
Stage II	5	1	0	4	0	5	0
Total	27	2	3	8	14	10 (37%)	17

TABLE XXIX. FIVE-YEAR RESULT OF 15 CASES OF ADENOCARCINOMA OF CERVIX

Nodes negative	11
*6 alive	
†5 dead	
Nodes positive	4
2 alive	
2 dead	

*One patient had no clinical recurrence for five years, but died of carcinomatosis six years after the operation.

†Three of the five patients developed recurrence late during the five years and died six years after the operation.

3. Carcinoma of the Cervical Stump.—

There were 23 cases of cervical stump carcinoma in this series, representing 6 per cent of all cases in which the cervix was involved. Meigs[20] reported a 2.1 per cent incidence of stump carcinoma in 1,218 cases of cervical cancers. Crawford and collaborators[21] reported a 5.7 per cent incidence of carcinoma

in 123 cervical stumps. Aldridge[22] concluded that from 6 to 7 per cent of all cancer of the cervix coming under treatment originated in cervical stumps.

In this series, the supravaginal hysterectomy had been done from 2 to 34 years previously. In 6 cases, it was done for metrorrhagia; in 5 cases for fibroids; in 2 cases for postmenopausal bleeding; in one case for pelvic inflammatory disease; and in 9 cases the reason was not stated in the history (Table XXX).

TABLE XXX. 23 CASES OF CARCINOMA OF CERVICAL STUMP

YEAR	AGE	TIME AFTER AND INDICATIONS FOR SUPRAVAGINAL HYSTERECTOMY	TYPE OF TUMOR	PREOPERATIVE RADIATION	NODE	RESULT
1940	44	19 years	Squamous	Yes	–	Well
1942	48	5 years	Squamous	–	–	Well
1943	41	16 years—Fibroids	Squamous	–	–	Well
1945	49	6 years—Metrorrhagia	Squamous	Yes	–	Well
1945	43	4 years—Metrorrhagia	Squamous	–	–	Well
1946	49	10 years—Fibroids	Squamous	Yes	–	Well
1948	50	3 years—Metrorrhagia	Adenocarcinoma	Yes	–	Well
1948	47	7 years	Squamous	–	–	Well
1948	47	14 years—Fibroids	Squamous	Yes	–	Well
1949	47	20 years	Squamous	–	–	Well
1949	52	5 years—Fibroids	Adenocarcinoma	–	–	Well
1949	57	2 years—Postmenopausal bleeding	Squamous	Yes	+	Dead
1949	49	4 years—Metrorrhagia	Squamous	Yes	+	Well
1949	36	4½ years	Squamous	–	–	Dead
1950	53	11 years—Metrorrhagia	Squamous	–	+	Well
1950	49	14 years—Pelvic inflammatory disease	Squamous	–	–	Well
1951	59	16 years—Metrorrhagia	Squamous	–	–	Well
1951	62	23 years—Postmenopausal bleeding	Squamous	Yes	+	Dead
1952	51	18 years	Squamous	–	–	Well
1952	68	30 years	Squamous	–	–	Dead
1952	56	10 years	Squamous	–	–	Well
1953	63	34 years—Fibroids	Squamous	–	–	Well
1953	49	23 years	Squamous	–	–	Well

Twenty-one cases were proved to be squamous-cell carcinoma, and 2 were adenocarcinoma. In none of these cases had cancer been demonstrated at the time of supravaginal hysterectomy.

TABLE XXXI. 23 CASES OF CARCINOMA OF CERVICAL STUMP

STAGE	NO. OF CASES	PREOPERATIVE IRRADIATION		NO PREOPERATIVE IRRADIATION		TOTAL	
		LYMPH NODES		LYMPH NODES		LYMPH NODES	
		POSITIVE	NEGATIVE	POSITIVE	NEGATIVE	POSITIVE	NEGATIVE
Stage I	16	1	5	1	9	2	14
Stage II	5	0	0	0	5	0	5
Stage III	2	2	0	0	0	2	0
Total	23	3	5	1	14	4 (17%)	19

TABLE XXXII. FIVE-YEAR RESULT OF 13 CASES OF CARCINOMA OF CERVICAL STUMP

Nodes negative	11
10 alive	
1 dead	
Nodes positive	2
1 alive	
1 dead	

Of these 23 patients with carcinoma of the cervical stump, 4, or 17 per cent, had positive lymph nodes (Table XXXI). Thirteen of these 23 patients were operated upon five or more years ago, and 11 are alive and well (Table XXXII).

4. Influence of Preoperative Irradiation on the Lymph Node Metastasis in Carcinoma of the Cervix.—

A summary was made to compare the incidence of lymph node metastasis between the patients with primary carcinoma of the cervix who had received preoperative irradiation and those who had not. The findings are rather inconclusive because of the variation in time and dosage.

Among the 344 patients with primary invasive carcinoma of the cervix, 85 had received preoperative irradiation; of these, 24, or 28 per cent, showed lymph node metastasis at the operation; 259 received no preoperative irradiation; of these, 64, or 25 per cent, had lymph node metastasis (Table XXXIII).

TABLE XXXIII. SUMMARY OF 344 CASES OF CARCINOMA OF CERVIX

	PREOPERATIVE IRRADIATION		NO PREOPERATIVE IRRADIATION		TOTAL	
	LYMPH NODES		LYMPH NODES		LYMPH NODES	
	POSITIVE	NEGATIVE	POSITIVE	NEGATIVE	POSITIVE	NEGATIVE
Stage I—231 Cases.—						
Squamous carcinoma	193	8	33	26	126	
Adenocarcinoma	22	1	3	4	14	
Stump carcinoma	16	1	5	1	9	41 (18%) 190
Stage II—109 Cases.—						
Squamous carcinoma	99	11	19	28	41	
Adenocarcinoma	5	1	0	4	0	
Stump carcinoma	5	0	0	0	5	44 (40%) 65
Stage III—4 Cases.—						
Squamous carcinoma	2	0	1	1	0	
Adenocarcinoma	0	0	0	0	0	
Stump carcinoma	2	2	0	0	0	3 1
Total 344	24 (28%)		61	64 (25%)	195	88 (26%) 256

5. Summary of End Result of All Primary Carcinoma of the Cervix.—

There were 193 patients with primary invasive carcinoma of the cervix who were operated upon and were followed for five or more years. This number includes 165 patients with squamous-cell carcinoma of the cervix, 15 with adenocarcinoma of the cervix, and 13 with carcinoma of the cervical stump. One hundred thirty-nine cases were classified clinically as being Stage I; 53 as being Stage II; and 1 as being Stage III.

TABLE XXXIV. SUMMARY OF FIVE-YEAR RESULT OF 193 CASES OF CARCINOMA OF CERVIX

	LYMPH NODES POSITIVE		LYMPH NODES NEGATIVE	
	ALIVE	DEAD	ALIVE	DEAD
Stage I—139 Cases.—				
Preoperative irradiation	46	6	4	30 (83%) 6
No preoperative irradiation	93	5	9	63 (80%) 16
Stage II—53 Cases.—				
Preoperative irradiation	25	2	8	11 4
No preoperative irradiation	28	4	10	12 2
Stage III—1 Case.—				
Preoperative irradiation	1	0	1	0 0
No preoperative irradiation	0	0	0	0 0
Total	193	17 (35%)	32	116 (81%) 28

Among this total number of 193 patients, 49 had regional lymph node metastasis, with a 35 per cent (17 patients) five-year survival rate, and 144 had no lymph node involvement, with an 81 per cent (116 patients) five-year survival rate (Table XXXIV).

Comment

Originally, the radical hysterectomy with regional lymphadenectomy in the clinics under study was restricted to a carefully selected group of patients in order to achieve a minimal operative mortality. This policy was dictated by the established position of radiotherapy. A high primary mortality at that time would have precluded further development of surgical treatment for cancer of the uterus. After nearly a decade of experience, it was evident that the risk of operation was low and the procedure effective. Accordingly, it was possible to extend the indications for radical operation so that more advanced cases and less robust patients were accepted in recent years. The low operative mortality in this series (1.7 per cent) is considered to be the result of improvement in the care of surgical patients. It is also noted that there was only one operative death among 344 operations for primary cancer of the cervix.

Radical hysterectomy with pelvic lymphadenectomy is essentially a procedure for cancer of the cervix. Some cases of carcinoma in situ in this series were originally diagnosed histologically as being invasive cancer. A review of the histological sections after the operation has placed them in the present category. We are now more conservative and require unequivocal histologic evidence of invasion before applying the radical procedure. Carcinoma in situ is now treated with a total hysterectomy with wide vaginal cuff resection.

Fistula formation is the *bête noire* of radical hysterectomy. In 9 per cent of the cases in this study a fistula developed. Of the 45 fistulas, 35 (78 per cent) involved the ureter. A satisfactory solution to this distressing problem has not been found. Fistula formation occurred approximately as frequently in 1953 as it did in 1939. Apparently, whatever improvement in technique was achieved had been offset by the progressive widening of the scope and radicality of the procedure. Undoubtedly adjacent tumor at times forces the removal of critical tissue.

The influence of preoperative radiotherapy on the development of fistulas is difficult to assess; 15, or 33 per cent, of the 45 patients in whom a fistula developed had received preoperative irradiation as compared with 29 per cent of the entire group. Although it is not reflected in the statistics, the patients who have fistulas after having received preoperative irradiation have a more difficult clinical course, if one may judge by the 9 patients in this study who had multiple fistulas, all of whom had had radiotherapy before the operation.

When a ureteral fistula develops, the patient will almost certainly lose the function of the involved kidney unless surgical intervention is taken. In only 8 patients out of 35 in this study was the kidney function preserved, and of these 6 had operative reimplantation into the bladder and one was saved by repeated ureteral dilatation. The technical difficulties of early operation are to be

balanced against the inevitable damage of infection and obstruction. Operation should, therefore, if possible, be undertaken within three to six weeks. If the gap between the viable ureter and bladder is excessive it can at times be bridged by a tube constructed from the bladder dome. If even this will not suffice, the ureter may be implanted in the adjacent large bowel.

Inevitably, there will be some patients in whom tumor tissue has not been completely extirpated. Of the 5 patients in this study in whom this occurred with tumor tissue remaining deep in the pelvis, 4 have died despite subsequent radiotherapy. The fifth patient is alive and well at five years.

Residual malignancy in the vagina is more easily recognized both in the surgical specimen and by subsequent vaginal smears. It is also much easier to eradicate by excision of more vaginal tissue. Among the 13 patients who have had incomplete removal of tumor from the vaginal cuff, 8 had subsequent total vaginectomy and 5 had no additional treatment. Of the 8 excised vaginal specimens, 3 showed the presence of invasive carcinoma, 2 carcinoma in situ, and the remaining 3 showed no demonstrable lesion. Failure to reoperate upon the patients when there is residual tumor at the vaginal cuff is rather serious in view of the fact that 3 deaths out of the 5 occurred in a brief period of time.

The incidence of metastasis to pelvic lymph nodes is remarkably constant in cancer of the cervix and the corpus. In carcinoma of the corpus, both the anatomical location of the tumor and the myometrial invasion by the cancer have great importance in lymph node metastasis. Among the patients with lesions confined to the corpus, 12 per cent had lymph node metastasis; but when the lesions involved both corpus and cervix, 50 per cent of the patients had lymph node metastasis. It was also found that lymph node metastasis was present in 4 per cent of the patients with corpus carcinoma limited to the endometrium in contrast to 45 per cent of the patients whose corpus cancer invaded the myometrium. The frequent lymph node metastasis in carcinoma of the corpus is somewhat surprising in view of the fact that comparatively favorable result has been achieved by simple hysterectomy alone.

The spread of benign and malignant endometrium to pelvic lymph nodes and to the ovaries affords interesting comparison. Among the 34 cases of pelvic endometriosis, 19, or 56 per cent, showed endometriosis in the ovaries, and 5, or 15 per cent, showed endometriosis in the pelvic lymph nodes. In the 47 cases of corpus carcinoma, ovarian metastasis occurred in 4, or a 9 per cent incidence, and lymph node metastasis in 11, or a 23 per cent incidence. This is at some variance with Javert's[23] finding in a larger series of cases. His data showed close parallelism between lymph node involvement of endometriosis and that of corpus carcinoma (29 per cent and 28 per cent, respectively). In addition, he found that, in the case of corpus carcinoma, the incidence of metastasis to lymph nodes is twice as high as to the ovaries.

The lymph nodes most commonly involved are the obturator, the common iliac, and the external iliac, with the last a poor third. All of the remaining pelvic nodes are occasionally involved, so that they cannot be ignored. The obturator nodes mentioned here lie at the bifurcation of the common iliac vessels between the external and internal iliacs, and adjacent to the obturator nerve.

The effect of preoperative irradiation on the incidence of lymph node metastasis in carcinoma of the cervix is rather inconclusive. The data showed that lymph node metastasis was present in 28 per cent of the patients who had received preoperative irradiation and in 25 per cent of the patients who received no irradiation before the operation.

Summary and Conclusions

The presentation is based on 473 cases of radical hysterectomy with pelvic lymphadenectomy performed by the staffs of the Vincent Memorial Hospital, the Massachusetts General Hospital, the Palmer Memorial Hospital, and the Pondville Hospital (the Massachusetts Department of Public Health) during a period of fifteen years from February, 1939, to December, 1953. The material is presented in two parts: the general information on patients who had radical hysterectomy with pelvic lymphadenectomy, and the patients having carcinoma of the cervix who were treated with radical hysterectomy.

The entire series of 473 cases included 294 cases of primary squamous-cell carcinoma of the cervix, 27 primary adenocarcinoma of the cervix, one case of leiomyosarcoma of the cervix, 23 cases of carcinoma of the cervical stump, 47 primary carcinoma of the corpus, 5 primary carcinoma of the vagina, 21 recurrent or residual carcinoma of the uterus (18 were squamous-cell carcinoma of the cervix and 3 were adenocarcinoma of the corpus), 34 carcinoma in situ of the cervix, and 21 referred cases in which cancer was found in the preliminary biopsy but there was no malignancy in surgical specimen.

Surgical complications occurred in 24 per cent of the patients and the operative mortality was 1.7 per cent.

Fistula formation as an operative complication occurred in 45 patients (9 per cent incidence); 35 of these fistulas involved the ureter. Thirteen (46 per cent) of the 28 uncomplicated ureterovaginal fistulas healed spontaneously between 1 and 10 months. Of these 13 cases, 3 had functional preservation of the involved kidney (one after repeated ureteral dilatations, 1 after reimplantation of ureter into the bladder, and one had no surgical intervention).

The value of radical hysterectomy with pelvic lymphadenectomy for carcinoma of the corpus is yet to be determined. The present series is regarded as an experiment that takes on added interest from the finding that there was lymph node metastasis in 23 per cent of the 47 cases.

There were 344 cases of primary invasive carcinoma of the cervix in this series. The number included 231 Stage I, 109 Stage II, and 4 Stage III cases. The incidence of lymph node metastasis in Stage I cases was 18 per cent, in Stage II cases 40 per cent, and in the entire group of 344 was 26 per cent. Of the 344 patients, 85 received preoperative irradiation. In these the incidence of lymph node metastasis was 28 per cent. Two hundred fifty-nine received no preoperative irradiation; of these 25 per cent had nodal metastasis.

One hundred ninety-three patients with carcinoma of the cervix were operated upon and followed for five or more years. One hundred and thirty-nine were in Stage I, 53 Stage II, and one was in Stage III. The five-year salvage rate in Stage I cases was 75 per cent, and that in Stage II cases was

54 per cent. Among the 193 patients, 49 had lymph node metastasis. Radical hysterectomy with pelvic lymphadenectomy salvaged 17 of these (35 per cent). One hundred forty-four had no lymph node metastasis; 116 of them (81 per cent) have been salvaged.

We are indebted to Drs. Langdon Parsons, Howard Ulfelder, Francis M. Ingersoll, Ward Gregg, and Fred Simmonds, whose cases operated upon are included here. Dr. Robert H. Fennell of the Department of Pathology, Massachusetts General Hospital, kindly reviewed many of the histologic sections.

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EXTENDED ABDOMINAL HYSTERECTOMY WITH PELVIC LYMPHADENECTOMY FOR CARCINOMA OF THE CERVIX

The Okabayashi Operation and Its Improved Techniques

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IN THE treatment of carcinoma of the cervix uteri, surgical approach in the form of abdominal extensive hysterectomy with pelvic lymph node dissection has received great attention in recent years. Meigs,[5] Brunschwig,[1] Twombly,[14] and Kelso[3] described their surgical techniques. In my previous paper[15] it was reported that the Okabayashi operation followed by postoperative radiation was more effective in the 5 year cure rate than radiation alone in Stages I and II.

The main features of the Okabayashi[8] operation are: (1) The posterior procedures, such as isolation of the rectum and resection of the cardinal and the uterosacral ligaments, are done prior to the anterior procedures. The better exposure of the cervix, bladder, and their surrounding areas makes possible an easier anterior manipulation. (2) Separation of the vesical part of the ureter and the lateral part of the bladder is systematic and with minimal bleeding. (3) Removal of the pelvic lymph nodes is also systematic and complete. These are the main points which distinguish this from Wertheim's operation.

From 1935 to 1952 I have performed this operation on 1,081 cases. From this experience I wish to describe the technique in detail.

Preoperative Care

Operation is indicated in the patient with Stage I and II cancer, who is under 60 years of age. Stage III is now seldom selected for the operation.

The general operability of the patients is carefully evaluated by routine diagnostic methods. Special attention is paid to the cardiac function which is tested by Kaufmann's diuresis method, Bickenbach's standing method, and by an electrocardiogram. The function of the kidney and liver is also examined in patients suspected of having renal or liver diseases.

Digitalis is administered routinely to patients daily in small amounts, the usual dose amounting to a total of 1.5 to 2.0 Gm. In anemic patients, with a hemoglobin of less than 60 per cent by the Sahli method, blood transfusion should be given once or twice during the preoperative week.

A vaginal douche is given daily with a solution of sulfonamides or antibiotics. Cauterization of the cervix was formerly performed in all cases im-

mediately before the operation for the purpose of disinfection and hemostasis. It has now been discontinued, because the administration of antibiotics is more effective for disinfection. Cauterization is now limited to cases with large cauliflower tumors.

Anesthesia

Spinal anesthesia with a Nupercaine derivative is generally used. Occasionally, especially in patients with weak cardiac function or with obesity, general anesthesia with ether is employed. The duration of the operation is approximately one and a half hours.

Description of Operation

1. Abdominal Incision.—

With the operator standing on the left side of the patient, a midline incision is made from the symphysis to the umbilicus. For adequate exposure the incision may be sufficiently long to permit a fist to enter the pelvic cavity, and must be close to the bony symphysis.

The patient is then placed in Trendelenburg position at an angle of forty-five degrees.

2. Examination of the Pelvic Organs.—

The intestines are packed out of the pelvic area with saline-soaked gauze pads. The pelvic peritoneum is examined for congestion, adhesions, metastases, or fluid in the cul-de-sac. Uterus, cervix, and urinary bladder, with their surrounding tissues, are carefully palpated. The pelvic lymph nodes are examined by palpation for enlargement and fixation. Last, any dilatation of the ureters is looked for.

Special attention is paid to the presence of scars and adhesions of the pelvic organs from inflammatory diseases, because they contribute to the difficulty of the operation. When extensive inflammatory changes preventing adequate and safe dissection of pelvic tissues are found, the operation should be abandoned in favor of radium and x-ray therapy. We have had poor results with Krönig's operation where the pelvic vessels are ligated to reduce the blood flow to the pelvic organs before radiation therapy. In inoperable cases, the abdominal wound is therefore closed without further manipulation.

3. Ligation and Incision of Round and Infundibular Ligaments.—

If the lesion is considered operable, the uterus is grasped with strong straight Péan forceps placed across the tubes, round ligaments, and part of the broad ligaments close to the uterus at each side. The handles of the forceps are tied and used as a retractor. In the past the body of the uterus was grasped with a vulsellum forceps, but this procedure was abandoned because of the danger of peritoneal contamination from leakage of purulent material from the puncture wounds in case of pyometra.

The left round ligament is ligated 1 to 2 cm. from the uterus and divided. This is in contrast to the other radical hysterectomy operations where the ligaments are incised close to the abdominal wall. It is our belief that metastases or infiltrations are seldom found in round ligaments or the adjacent peritoneum, and the importance of preserving the peritoneum for peritonization outweighs the danger of leaving behind tumor tissue which happens infrequently. The left infundibulopelvic ligament is picked up and ligated 1 cm. from the pelvic brim, for at this point the ureter is well out of the way. The uterine end of the ligament is then clamped and incised between the ligature and the clamp. The leaves of the broad ligament between the round and

infundibulopelvic ligaments are incised, and the incision of the anterior leaf is carried through the vesicouterine fold.

The same procedure is repeated on the right side.

4. Removal of Normal Ovaries for Transplantation to the Rectus Muscle.—One normal ovary in patients between the ages of 30 and 50 (both normal ovaries in the case of a young patient below the age of 30) is removed for later transplantation to the rectus muscle. The ovaries are placed in a saline-soaked gauze pouch which is kept at body temperature in the iliac fossa during operation. Abnormal and atrophic ovaries are not used.

5. Isolation of Uterine Artery and Ureter.—

The leaves of the left broad ligament are separated by blunt and sharp dissection through the intervening loose areolar tissue. The uterine artery, which is identified as coursing from the hypogastric artery to the uterus, is freed at its hypogastric origin, doubly ligated, and cut.

The left ureter is identified lying on the posterior leaf of the broad ligament, is carefully freed with its surrounding periureteral sheath from the pelvic brim to the point where the uterine artery crosses anteriorly and enters the thick paravesical tissue. Special effort is made not to bare the ureter by dissecting its sheath.

The posterior leaf of the broad ligament is now incised approximately 1 cm. from, and parallel with, the uterus down to the uterosacral ligament.

Procedure 5 is repeated on the right side.

6. Separation of the Rectum.—

The uterus is drawn upward and toward the symphysis. Tension is made on the rectum by pulling it cephalad, thus reducing the size of the posterior cul-de-sac and bringing into view the rectovaginal fold of the peritoneum, which is well below the uterine attachment of the uterosacral ligaments. The peritoneum is incised in the midline at this point. Since loose areolar tissue lies between the rectum and the vagina in the midline, their separation is easily performed. This dissection is carried down to at least 2 cm. below the cervix. If the posterior vaginal wall reveals infiltration at the time of the gynecological examination, the dissection must be carried down at least 2 cm. below the lowest point of the infiltration. During the separation of the rectum, the superficial uterosacral ligaments are incised without ligation at a point midway between the uterus and the rectum.

7. The Exposure of the Pararectal Fossa and the Medial Surface of the Right Cardinal Ligament.—

The rectum is retracted laterally to the left. Lateral to the right uterosacral ligament, which has been incised, the right pararectal fossa is exposed by blunt dissection of its loose areolar tissue. The space is ovoid in shape and measures approximately 5 by 6 cm. in diameter. It is bound laterally by the medial surface of the cardinal ligament, medially by the rectum and the stump of the uterosacral ligament, posteriorly by the sacrum, anteriorly by the posterior wall of the vagina, and inferiorly by the pelvic floor.

8. The Exposure of the Right Paravesical Fossa and the Isolation and Incision of the Right Cardinal Ligament.—

The uterus is now pulled upward and to the left. The lateral stump of the uterine artery is identified. An entrance into the paravesical fossa containing loose areolar tissue is found just anterolateral to this stump. The space is easily entered by pushing the index finger into the area. By blunt finger dissection areolar tissue is freed. This reveals a triangular cavity which is bound posteromedially by the lateral surface of the cardinal ligament, anteromedially by the bladder, and laterally by the pelvic wall. The cardinal ligament separates the two fossae. The inferior part of the cardinal ligament,

however, is thinned out so that by sharp dissection it can easily be penetrated and the opening widened; thus the thick cardinal ligament appears as a wide bridge attached to the cervix and the lateral pelvic wall (Fig. 1). Before clamping and incising the cardinal ligament, strands of strong fibrous tissue which fan from its medial surface to the pelvic attachment are cut by repeated small bites with scissors in the area close to the pelvic wall. This re-

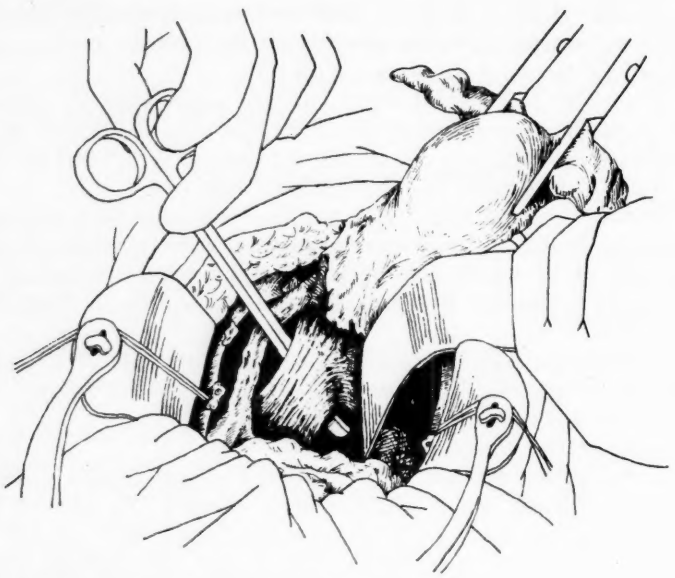

Fig. 1.—Isolation of the left cardinal ligament. (1)
The uterus is pulled upward and to the right. The rectum is retracted to the right. The left cardinal ligament is isolated, and after cutting of the thin membrane of the inferior part, it appears like a bridge, which reaches from the cervix to the pelvic wall. The scissors are inserted into the left paravesical fossa and the top is seen from the pararectal fossa.

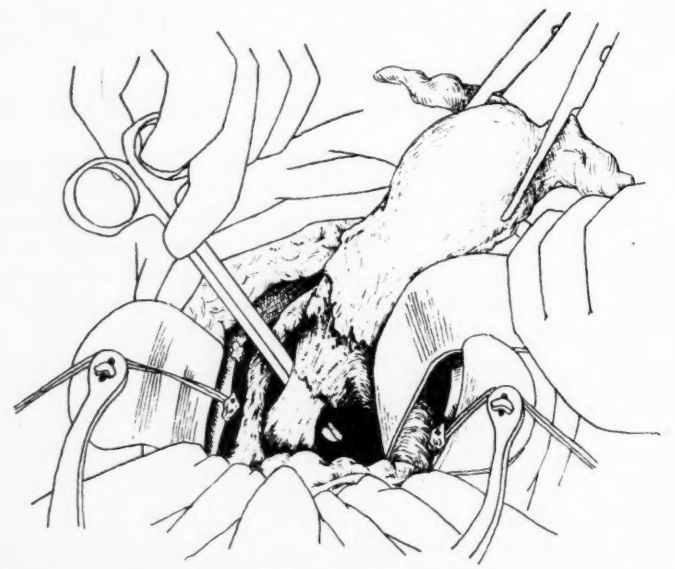

Fig. 2.—Isolation of the left cardinal ligament. (2)
Before clamping and incising the cardinal ligament, strands of strong fibrous tissue on the surface are cut by small bites in the area close to the pelvic wall.

duces the thickness of the ligament at the point of incision (Fig. 2). No large blood vessels are encountered on the medial surface of the ligament. With the ureter, which during the dissection lies anteromedially and is now displaced laterally, the ligament is doubly clamped near the pelvic wall with 2 strong curved Péan forceps laid parallel and incised between the clamps (Fig. 3). The lateral stump of the ligament is ligated with a strong silk suture. This

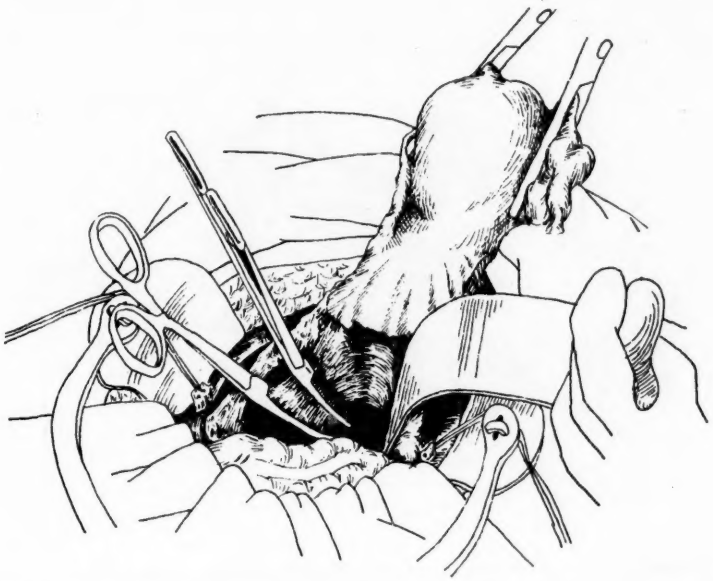

Fig. 3.—Incision of the left cardinal ligament. (1)
The left cardinal ligament is doubly clamped near the pelvic wall with strong curved Péan forceps.

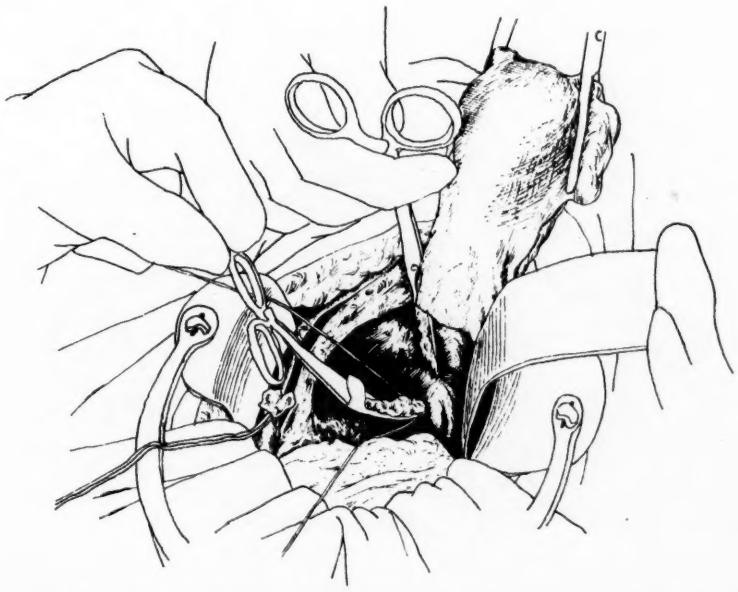

Fig. 4.—Incision of the left cardinal ligament. (2)
After incising the left cardinal ligament, the lateral stump is ligated with a strong silk suture. The cutting of this ligament results in the union of the paravesical and pararectal fossae to form a single large cavity.

ligament at the point of incision measures about 2 cm. in width. The cutting of this ligament results in the union of the pararectal and paravesical fossae to form a single large cavity (Fig. 4).

Procedures 7 and 8 are repeated on the left side. (All figures show manipulation on the left side.)

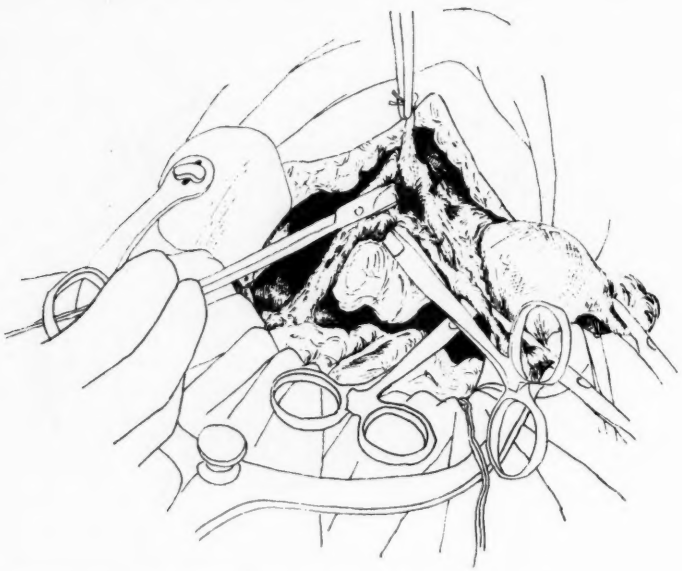

Fig. 5.—Isolation of the vesical part of the left ureter. (1)

The medial stump of the left uterine artery is picked up and traction is made upward. A canal is found through which the ureter courses to the bladder. This canal is enlarged with the flat surface of the scissors.

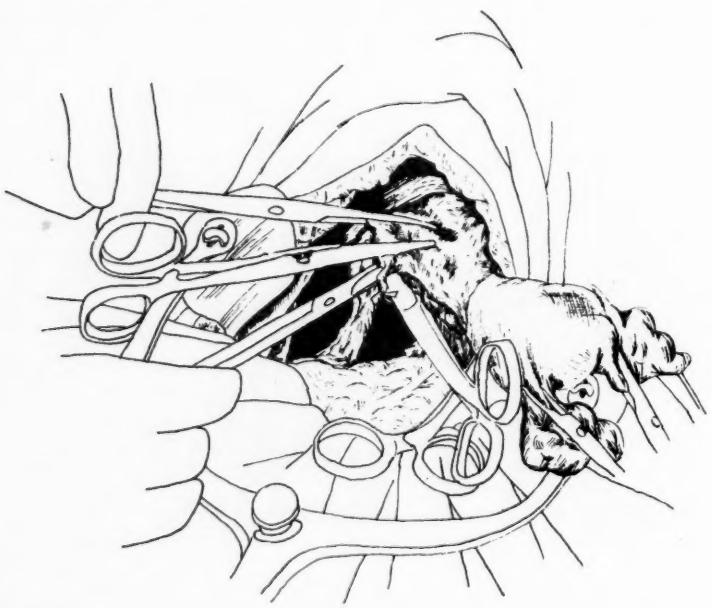

Fig. 6.—Isolation of the vesical part of the left ureter. (2)

The medial stump of the left uterine artery is pulled cephalad and the vesicouterine ligament (superficial layer) is clamped with a fine curved Péan forceps and a straight fine forceps and the tissue between incised.

9. The Separation of the Urinary Bladder.—

In contrast to Wertheim's and most other radical hysterectomy operations, the bladder and ureters are isolated after the posterior dissection, which permits the bladder and ureters to be drawn out of the deep pelvis when traction on the uterus is made cephalad, thus facilitating their dissection, by better exposure. The peritoneum at the vesicouterine junction has been pre-

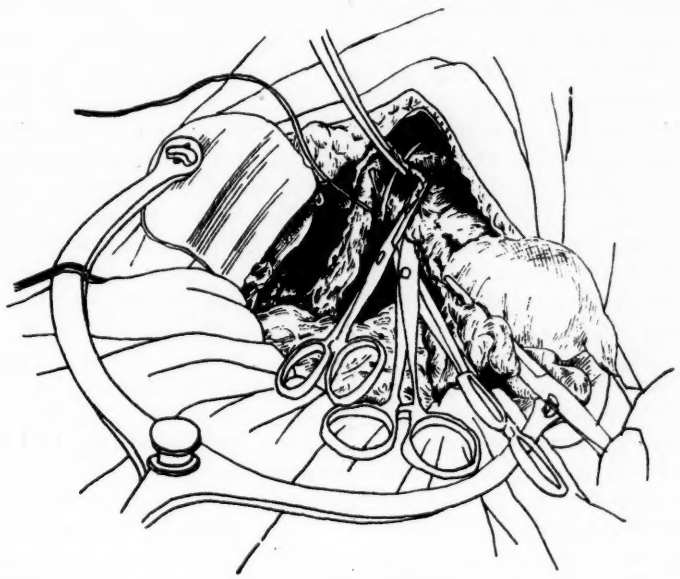

Fig. 7.—Isolation of the vesical part of the left ureter. (3)
The lateral stump of the superficial layer of the left vesicouterine ligament is ligated with a suture.

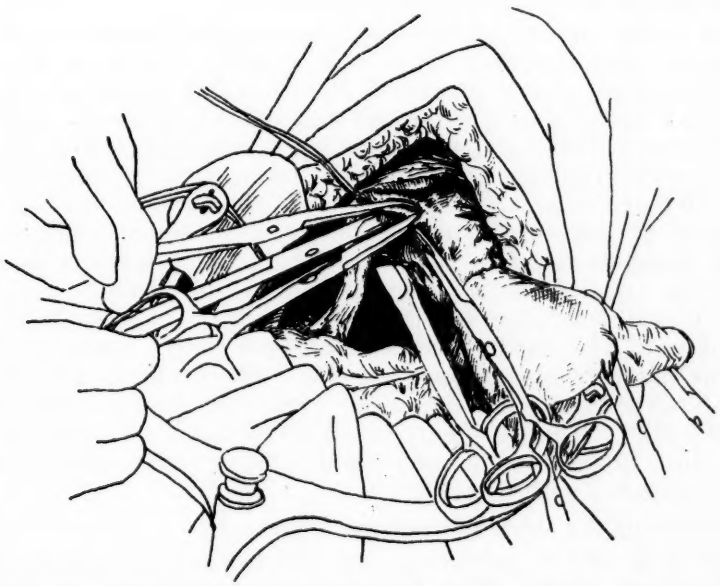

Fig. 8.—Isolation of the vesical part of the left ureter. (4)
The second clamp is laid on the superficial layer of the left vesicouterine ligament. This layer is cut in small bites, so as to let the ureter keep its natural course without kinking. With 2 to 3 ligatures this layer is incised completely.

viously incised. By blunt dissection, the bladder is easily separated from the cervix and the vagina in the midline so as to admit two fingers. When the dissection is kept to the midline area, no excessive and troublesome bleeding should be encountered. The bladder is freed at least 2 cm. below the cervix, and, if the anterior vaginal wall is involved, the separation must be carried down to at least 2 cm. below the inferior margin of the infiltration.

10. Isolation of the Vesical Part of the Ureter.—

The ureter from the pelvic brim to the uterine artery has been freed previously. The medial stump of the left uterine artery is picked up with forceps and traction is made upward (Fig. 5). This places the tissue lying anterior to the ureter on a tension and permits ease of exposure of the canal through which the ureter courses to the bladder. The paravesical connective tissue (i.e., the superficial layer of the vesicouterine ligament) lying anteriorly contains the vesical vascular plexuses; posteriorly lies the deeper layer of the vesicouterine ligament. Before the beginning of the isolation of the ureter in this area, the ureteral artery arising from the uterine artery is sometimes encountered; this vessel must be ligated and cut if present. This canal or tunnel is carefully enlarged by following the ureter laterally with a flat surface of the blunt long scissors (Fig. 5). Then the medial stump of the left uterine artery is turned cephalad (Fig. 6) and the superficial layer of the vesicouterine ligament is clamped with a fine curve Péan forceps with the tip facing toward the cervix; a straight fine forceps is placed medial to the above clamp and the tissue between incised. The lateral stump is ligated with a suture (Fig. 7). Only a small amount of the tissue is clamped, cut, and ligated at a time until the ureter enters the bladder (Fig. 8). Care must be taken not to injure the ureter during this procedure. Taking small bites of this paravesical tissue is important in preventing the kinking of the ureter, since a single large ligation frequently results in a ureteral kink with obstruction of the urinary flow. Ureteral fistula most commonly occurs in this area.

11. Division of the Vesicouterine Ligament.—

Incision of the superficial layer of vesicouterine ligament over the ureter to its entrance into the bladder reveals a small triangular space (Fig. 9) medial to the ureterovesical junction. By blunt dissection, one enters a space which is bound medially by the vaginal wall, anteriorly by the bladder, anterolaterally by the ureter and lateral portion of the paravesical tissue (superficial layer), and posterolaterally by the vesicouterine ligament (deep layer) (Fig. 10). When the areolar tissue is bluntly separated with the finger the inferior aspect of this space (toward the pelvic floor) is contiguous with the paravesical fossa so that the vesicouterine ligament is likewise a bridge of tissue between the lateral inferior margin of the bladder and the cervix (Fig. 11). The scissors placed in this space push the bladder laterally and the uterine stump of the cardinal ligament is retracted medially, placing the vesicouterine ligament on tension (Fig. 12). The ureter is attached by a few strands of fibrous tissue to the superior border of the ligament, is freed and displaced laterally. The ligament is now doubly clamped with straight Péan forceps as close to the bladder as possible and cut (Fig. 12). The stump of the bladder is ligated with a suture.

12. Division of the Deep Uterosacral Ligament.—

The uterus is now retracted upward and toward the symphysis, exposing the posterior deep pelvis. With the uterus under tension, the deep layer of the uterosacral ligament is seen (Fig. 13). This tissue is ligated midway between the cervix and the rectum and incised, thus freeing the uterus and vagina completely from their posterior attachments.

13. Division of the Paravaginal Tissue.—

The uterus is again pulled cephalad and the cervical stump of the cardinal ligament is placed under tension in the same direction. This places the paravaginal tissue (paracolpium) under tension. One or two ligatures are placed at the margin of the vagina at the point where the vagina is to be incised

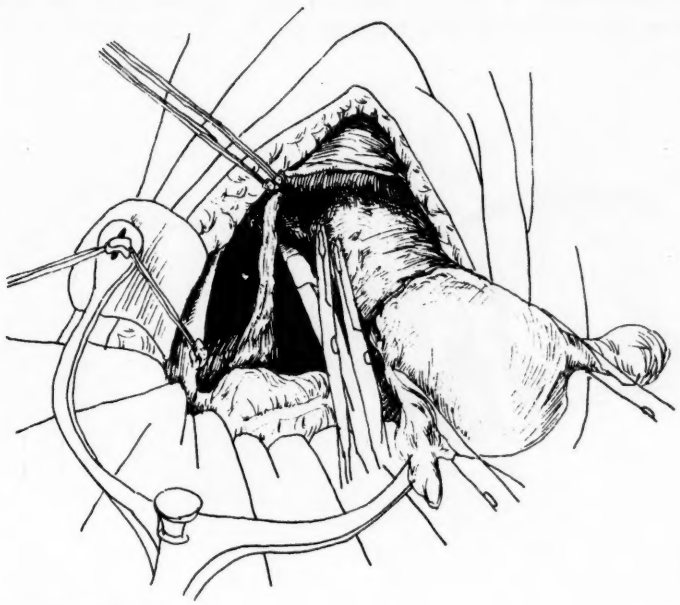

Fig. 9.—Triangular space. (1)

After incision of the superficial layer of the left vesicouterine ligament, a small triangular space is found, which is bound medially by the vaginal wall, anteriorly by the bladder, anteromedially by the ureter and posterolaterally by the deep layer of the vesicouterine ligament.

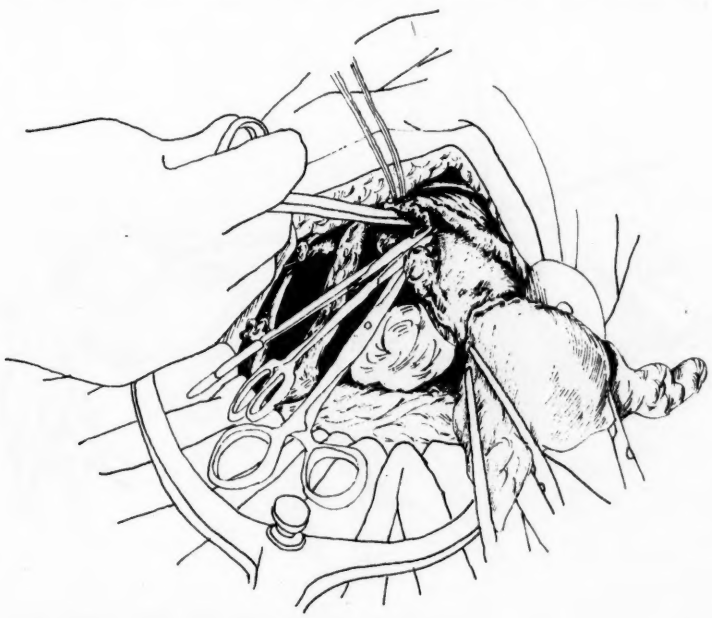

Fig. 10.—Triangular space. (2)

This triangular space is widened by the scissors inserted into it and pushing the bladder laterally and then pulling cephalad the deep layer of the vesicouterine ligament.

(Fig. 14). The tissue is cut. This frees all the tissues attached to the vagina, cervix, and uterus on the left side. The right-angle forceps is fixed on the vaginal margin.

Procedures 10, 11, 12, and 13 are repeated on the right side.

14. Removal of the Specimen—Open Method.—

A clean gauze pad is placed behind the vagina and the uterus. Meanwhile the nurse has removed the vaginal pack. At the level of the two right-

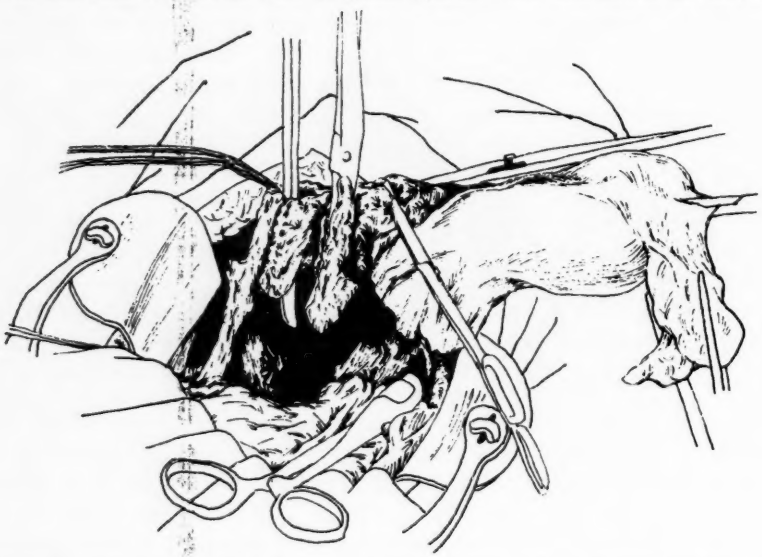

Fig. 11.—Division of the left vesicouterine ligament (deep layer). (1)
The scissors deeply inserted into this triangular space push the bladder laterally. The uterine stump of the cardinal ligament is retracted medially, so that the deep layer of the left vesicouterine ligament is placed on tension (as shown in Fig. 12).

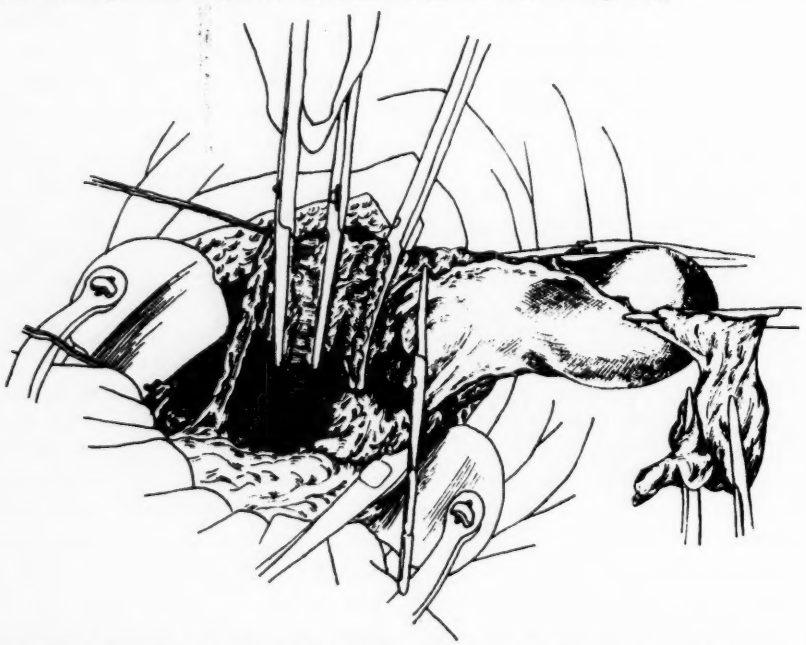

Fig. 12.—Division of the left vesicouterine ligament (deep layer). (2)
The deep layer of the left vesicouterine ligament is likewise a bridge of tissue between the lateral inferior margin of the bladder and the cervix.

angle forceps marking the limit where the vaginal incision is to be made, the electrocautery is used to open the anterior wall of the vagina. The edge of the vaginal wall is immediately clamped with Kocher forceps at three points. The vagina is cleansed with 1 per cent Lysol-soaked gauze. Following this, the posterior vaginal wall is incised, freeing the specimen.

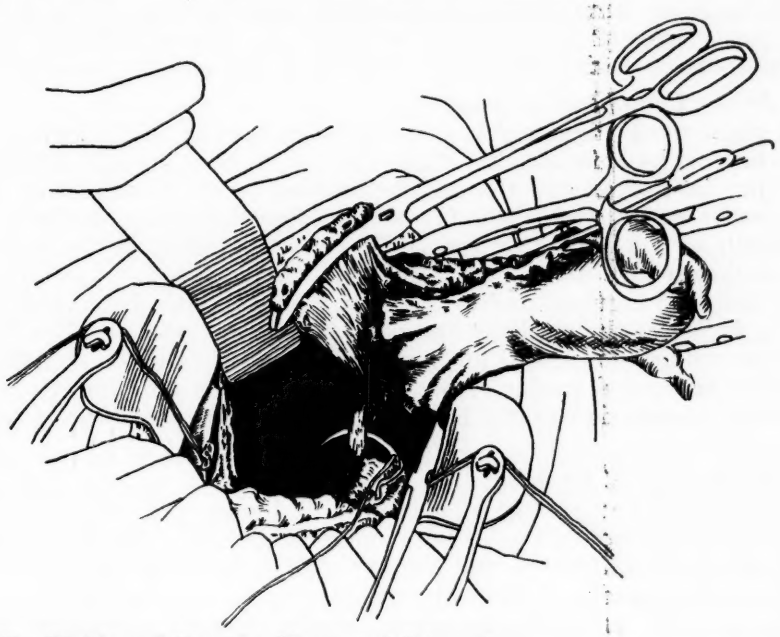

Fig. 13.—Division of the deep uterosacral ligament.

The uterus is retracted upward and toward the symphysis and the uterine stump of the left cardinal ligament is stretched anterolaterally, then the deep layer of the left uterosacral ligament becomes evident. This is ligated midway between the cervix and the rectum.

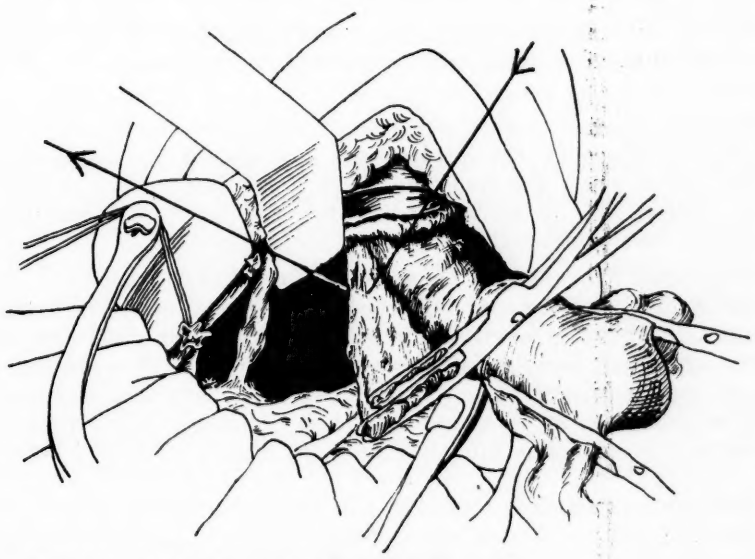

Fig. 14.—Division of the left paravaginal tissue.

The uterus is pulled cephalad and the uterine stump of the left cardinal ligament is stretched laterally and upward. Then the left paracolpium is placed on tension. One or two ligatures are placed to the margin of the vagina at the point where the vagina is to be amputated.

15. Closure of the Vaginal Stump.—
The margin of the incision is painted with Lugol's solution and the vaginal closure is completed by interrupted sutures with the invagination of the mucosal edges.

16. Fixation of the Urinary Bladder to the Vaginal Stump.—
If there is no hemorrhage after careful examination of the pelvis, three interrupted sutures (2 lateral and 1 midline) are placed through the bladder peritoneum, the posterior wall of the vaginal stump and the rectal peritoneum.

17. Pelvic Lymphadenectomy.—
The right round ligament is grasped with forceps and retracted laterally and upward. The inferomedial iliac and hypogastric lymph nodes and the surrounding fat and areolar tissues are removed by sharp and blunt dissection. The obturator nodes with their fat and areolar tissue are similarly removed to the depth of the obturator fossa. The distal portion of the common iliac and the external iliac nodes and tissue are next removed, followed by the removal of the deep inguinal nodes. Finally, the small parametrial nodes around the pelvic stump of the cardinal ligament and the sacral nodes are removed.

The procedure is repeated on the left side. Complete removal of all lymph nodes, whether normal in size or swollen, and the surrounding fat and areolar tissues with lymphatic vessels is very important in obtaining a permanent cure.

18. Paracoccygeal Drainage.—
A moderately firm rubber tube, 0.5 cm. in diameter, is placed 2 cm. lateral to the tip of the coccyx on one or both sides. The rubber drain is grasped with a strong curved Péan forceps and forced through the pelvic floor to a point on the skin approximately 2 cm. anterolateral to the tip of the coccyx. The overlying skin and subcutaneous tissue are cut from the outside to permit its passage.

The drain is used only when hemorrhage is not completely controlled because of oozing or when infection is suspected.

19. Antibiotics.—
Five cubic centimeters of a solution containing 200,000 units of crystalline penicillin and 20 per cent sulfonamides is sprayed on each side of the area of operation.

20. Peritonization.—
The lateral edges of the peritoneum are closed by continuous running suture. Before its ends are tied, the peritoneum is gently but firmly pressed against the pelvic wall to reduce the retroperitoneal space and to encourage adhesions of the two surfaces.

21. Abdominal Closure and Transplantation of the Ovary.—
The abdominal peritoneum is closed by running continuous suture.

The normal ovary is hemisectioned and sutured so that the cut surfaces are on the outside. Visible follicles are punctured. The rectus muscle at the level of the umbilicus is separated and the ovary transplanted into this space. If both ovaries are transplanted, one is placed in the right and one in the left rectus muscle. The muscle edges are closed with two interrupted sutures.

The abdominal wound is closed in the usual manner.

Care During Operation

The quantity of bleeding during the operation is measured by weighing the blood-soaked gauze at regular intervals, for example, every 10 minutes

Blood transfusion or infusion of 5 per cent dextrose solution is given to cover the loss of blood. Recently the amount of bleeding was measured in 122 cases and the results are presented in Table I.

TABLE I. TOTAL AMOUNT OF BLEEDING (122 CASES)

AMOUNT (C.C.)	NO. OF CASES
0- 100	2
100- 200	13
200- 300	34
300- 400	31
400- 500	14
500- 600	10
600- 700	8
700- 800	4
800- 900	3
900-1,000	1
1,000-	2

Postoperative Care

An indwelling catheter is placed in the bladder for a period of about 10 days. The quantity of urine is measured every 3 hours after the operation for 3 days and is recorded on a chart. This method of recording is very simple and useful as an indicator of the cardiac function after the operation. In favorable cases the urinary output progressively increases, but in the presence of cardiac insufficiency it may decrease. Following the injection of cardiac stimulants, an increased urine output is again observed.

Blood transfusion is given in quantity sufficient to cover the loss of blood during the operation. Cardiac stimulants, vitamin K, and antibiotics are administered in a planned manner for 3 days after the operation.

The most common complications are cystopyelitis and retroperitoneal abscess, formerly called "parametritis." To prevent urinary infections, the examination of the urine is done daily and as stated previously sulfonamides or antibiotics are routinely given as prophylactic measures.

The diagnosis of retroperitoneal abscess is not as easily made as cystitis or pyelitis. A rectal examination should be performed to palpate both sides of the vaginal stump, when the fever rises above 103° F. or an induration is palpated externally on the inguinal region. Whenever paravaginal induration is detected by rectal palpation, an abscess is suspected. An exploratory puncture with a long needle is then attempted at the corner of the vaginal stump. If pus is obtained, an opening must be made at the corner of the stump by cutting a single suture from this area. Aspiration of the contents and instillation of a small dose of antibiotics may be carried out. By this procedure one can easily cure the abscess, which has been an annoying complication in the past.

The ease with which such an abscess may be treated is one of the reasons why it is preferable to close the vaginal stump at the operation. The other reason is because of the potential danger of infection from the vagina, as has been proved by bacteriological study of the parametria and the vagina during

operation (Sato[11] and Takahara[12]). The retroperitoneal cavity, including the parametrium, is almost sterile and free of pathogenic bacilli, while the vagina always contains pathogenic cocci and bacilli even after thorough disinfection. Communication between the retroperitoneal cavity and the vagina through a drain cause the danger of provoking infection. Complete closure is felt to be much safer. When drainage is necesssary, a paracoccygeal drain is inserted penetrating the pelvic muscular floor (Kobayashi[4] and Ogino[7]), as described previously. It is taken out in 24 or 48 hours according to the quantity of wound fluid.

The primary mortality was 7.2 per cent according to the previous report, which included deaths immediately after the operation and deaths during the postoperative convalescence in the hospital. Since the antibiotics came into use in 1950, the primary mortality has been reduced to 2.3 per cent (12:525 cases).

Ureterovaginal fistulas occurred in 3.8 per cent in the earlier series, but this figure has also been reduced to 2.1 per cent since 1950 (11:525).

Bladder Paresis

The indwelling catheter is removed on the tenth day, and the ability to void spontaneously is observed. If it is possible, the residual urine is measured by catheterization after urination in order to compare the quantity of the spontaneous and residual amounts. As time elapses, the urine voided spontaneously becomes greater in quantity till it surpasses the residual. The test is then discontinued. During this period, heating by diathermy over the bladder, injection of strychnine in minimal doses and exercises for the bladder are employed to improve bladder muscle tone. On or about the twentieth day after the operation the bladder has regained the greater part of its function, but at least several months, on the average six, are required before the paresis is completely cured.

Postoperative Radiation

Radiation therapy is begun about the third week after operation in all cases as a prophylaxis against recurrence. The dosage was described in the previous paper.[15] The entire postoperative convalescence averages 40 days. Two months after discharge from the hospital the first follow-up examination is made and thereafter it is repeated in a planned manner.

Autotransplantation of the Ovary

In the combined treatment by operation and postoperative radiation, the problem of the preservation of ovarian function is quite important. If the ovaries are left in their original position, they will be exposed to radiation and subsequently destroyed. To avoid this and to maintain the function, one or both ovaries should be transplanted outside the areas to be radiated if the patients are less than 50 years of age. This procedure has been studied in Japan by many authors (Ohno,[10] Hiraishi and Yokoo,[2] Tamura,[13] Moriya,[6] etc.)

The histological research of Tamura[13] first revealed that in carcinoma of the cervix, no metastasis to the ovary occurs, quite contrary to the situation in carcinoma of the uterine body, in which the ovary lies in the route of the cancer through the lymphatics. In case of carcinoma of the cervix, especially in its early stages, the ovary lies out of the path of progress of the cancer. In my own study of 483 cases from 1938 to 1949, no metastatic tumor has been discovered in the transplanted ovaries.

Moriya[6] investigated the urinary estrogen after the transplantation and found that the planted ovary continued to function. The duration of the function depends on the age of the patient on one hand and the condition of the ovary on the other. It is believed that in one to three years the ovary degenerates gradually and is finally resorbed. During this period, castration symptoms are prevented. In these 483 cases of ovarian transplantation castration symptoms were prevented in 85 per cent (200:234) and atrophy of the genitals prevented in 70 per cent (165:234). In contrast to these operative cases, the patients in the radiation group, in which both ovaries had been exposed to x-rays, showed marked atrophy of the genitals and also castration symptoms.

In the patient under 50 years of age, ovarian transplantation is therefore a recommendable procedure. When the patient is young, for example, below 30 years of age, both ovaries should be used for transplantation.

I wish to express my thanks to Dr. M. Suzuki, gynecologist at the Atomic Bomb Casualty Commission, Hiroshima, for calling at my clinic to observe 4 cases of this operation in order to review this paper. I wish also to express my deep sorrow upon the death of Dr. H. Okabayashi, my beloved teacher, who passed away on Jan. 17, 1953.

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CARCINOMA OF THE CERVIX UTERI TREATED AT THE AMERICAN ONCOLOGIC HOSPITAL, 1929 TO 1949*

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A PREVIOUS report[1] summarized the results obtained in the treatment of carcinoma of the uterine cervix at the American Oncologic Hospital. The group studied at that time consisted of 142 patients, 98 of whom had been followed for a period of five or more years. The five-year survival rate of all patients treated was 24 per cent. These patients all had histologically proved invasive carcinomas of the cervix uteri and all were treated by means of irradiation.

The American Oncologic Hospital is a fifty-five-bed institution which deals primarily with patients who have neoplastic disease or who are suspected of having malignant disease. Very few of the patients come of their own accord to the hospital. The majority of the patients are sent by physicians or other hospitals when a diagnosis of carcinoma is made or is suspected.

Material

The present report considers all patients seen at the American Oncologic Hospital with a histologically proved diagnosis of carcinoma of the cervix uteri during the twenty-year period, Jan. 1, 1929, to Jan. 1, 1949. During this time 319 patients were examined with a view to treatment. Patients with carcinoma in situ are not included in this report. Ten of these patients were not treated at the Oncologic Hospital, either refusing therapy completely or going elsewhere.

Twenty-one patients had received their primary treatment elsewhere (Group V cases). Only one of these patients survived five or more years, a survival rate of 4.8 per cent.

This report deals only with the 288 patients treated primarily at the American Oncologic Hospital. The follow-up in these cases was 95 per cent.

In the previous report all patients were classified entirely by the Schmitz grouping. For the preparation of this paper it has been necessary to re-evaluate as accurately as possible the extent of the patient's disease on the basis of the International Classification. This changeover has not been difficult with Stage I and Stage IV patients but has required considerable thought in the attempt properly to classify patients in the Stage II and Stage III categories.

Race, Age, and Parity

The ages of the patients varied from the youngest at 21 years of age to the oldest at 85 years of age (Fig. 1). The greatest incidence of cervical cancer occurred during the age period from 41 to 50 with 100 patients (34.6 per cent) in this category. As has previously been emphasized by Scheffey,[2] it is signifi-

*Presented at a meeting of the Obstetrical Society of Philadelphia, Jan. 7, 1954.

cant to note the relatively high percentage of patients 40 years of age or younger with carcinoma of the cervix. In this series there were 94 such patients, an incidence of *32.6 per cent.*

In our clinic 69.3 per cent of the patients belonged to the white race, of whom only 1 per cent (3 patients) were Hebrew in origin. The remaining 30.7 per cent were Negro, a greater percentage than is usually found in the average general hospital in the Philadelphia area. There is a gradually increasing percentage of Negro patients at the American Oncologic Hospital as time goes on.

Fourteen and five-tenths per cent of the patients were nulliparous, 85.5 per cent parous. The greatest parity was thirteen.

Fourteen of the 288 cases were adenocarcinomas, an incidence of 4.9 per cent. The remainder were squamous-cell carcinoma.*

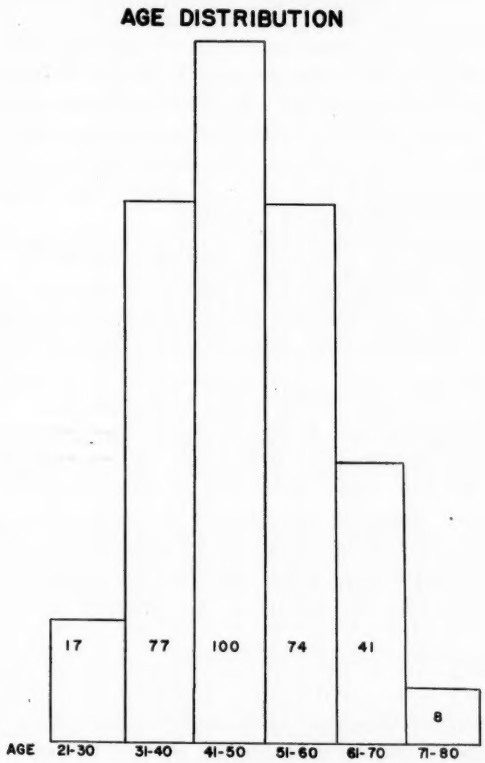

Fig. 1.

Symptoms

Vaginal bleeding was the most common chief complaint that was elicited as the reason for which the patient first sought medical advice. There were 136 patients who were first seen by a physician because of irregular vaginal bleeding, 47 patients had postmenopausal bleeding, and 15 patients volunteered the information that the bleeding was first noticed following coitus.

Vaginal discharge was the second most common symptom which caused the patient to seek medical attention. There were 40 patients in this category. In most instances the discharge was described as being dark yellow or brown in color.

*Diagnoses made by Drs. J. McFarland, E. Ciccone, and A. Donnelly.

There were 13 patients whose chief complaint was pain. In 10 of these cases the pain was abdominal in location and in 3 instances the pain was localized in the back.

One patient, a spinster in her sixties, was examined because she was unable to urinate. She was found to have a Stage IV lesion that had compressed and invaded the urethra. She survived less than a month after admission to the hospital.

In only one instance were there no pelvic symptoms. This patient was a 36-year-old parous patient who was hospitalized elsewhere because of pleurisy. On physical examination a Stage I lesion was detected and she was referred to the Oncologic Hospital for management.

In the remainder of the cases it was not possible to designate any single symptom alone as being responsible for the patient's first visit to the hospital.

Associated Conditions

A. The most frequently associated condition in this series which might be of significance was the occurrence of a positive Wassermann test in 13 patients, an incidence of 4.5 per cent. A disproportionately high percentage of patients with carcinoma of the cervix and carcinoma of the tongue have syphilis, although this is not true of any other major form of cancer. Levin and his co-workers[3] found 3.9 per cent of a series of 930 patients with carcinoma of the cervix had evidence of syphilis.

B. Diabetes mellitus, a common finding in patients with endometrial cancer, was present in 7 patients, 2.4 per cent.

C. Six patients had marked hypertension, one patient had severe rheumatic cardiovascular disease, and one patient, still living, has a large aortic aneurysm.

D. Five patients, 1.7 per cent, also had primary carcinomas elsewhere in the body. Two patients had primary adenocarcinoma of the endometrium which was present at the time the diagnosis of cervical carcinoma was made. Primary carcinoma of the anus occurred in one patient, and primary rectal carcinoma and primary sigmoid carcinoma developed in another patient after the completion of therapy for carcinoma of the cervix uteri.

E. Lymphopathia venereum with marked rectal stenosis, acute gonorrheal salpingitis, and a large mixed tumor of the parotid were each present in one patient.

F. Marked obesity (over 300 pounds) occurred in two patients. Patients of this weight present a most difficult problem from the therapeutic standpoint, since it is virtually impossible to deliver an adequate dosage by means of x-irradiation in the tumor area because of the depth of tissue that must be penetrated. Fortunately both these patients had relatively early lesions and have survived more than five years.

G. Two of the patients had complete procidentia (0.7 per cent). The low figure conforms with the expected rarity of the condition. One of these patients had worn a pessary with varying degrees of success at intervals during a twenty-five-year period. Despite the fact that the cervix was completely exposed in both patients, both had advanced disease when first seen.

Previous Pelvic Surgery

Sixty of the patients (20.8 per cent) had previously been operated upon for pelvic difficulties. By far the largest number, 28, or 46.6 per cent, had had supravaginal hysterectomies. This group will be discussed in greater detail in a later portion of this presentation.

Six of the patients previously had had vaginal hysterectomies with prompt evidence of unarrested disease. In an earlier paper[4] the poor prognosis in such patients has been stressed.

Six of the patients had trachelectomies performed, one in conjunction with a Watkins interposition operation. The latter patient's original surgery was done by a competent gynecologist, the unsuspected Stage I lesion was discovered on routine histologic examination, and the patient is living and well twelve years after her radiation therapy.

Six patients had pelvic plastic repair operations in conjunction with diagnostic curettage. As far as can be determined no cervical biopsy was performed in any of these cases.

Four patients had previous bilateral salpingo-oophorectomies, one of them in conjunction with amputation of the cervix. Cianfrani[5] recently reported a series of 130 patients who had had bilateral salpingo-oophorectomies with the subsequent development of 11 (8 per cent) carcinomas of the cervix, and 8 (6 per cent) carcinomas of the endometrium. I believe the incidence of cancer in Cianfrani's presentation is higher than the true incidence, since the original pelvic surgery in certain instances was noted after a survey of patients with proved pelvic malignancy was made.

Three patients had previously had a unilateral salpingo-oophorectomy.

A bilateral salpingectomy, an ovarian cystectomy, an exploratory pelvic laparotomy, and an incision and drainage of a pelvic abscess had each been performed once. One patient had had a complete abdominal hysterectomy and bilateral salpingo-oophorectomy. Carcinoma of the cervix was found in the removed specimen, but almost a year elapsed before she was referred to the Oncologic Hospital for irradiation therapy. This patient survived less than two years.

A myomectomy had been performed on a 54-year-old patient fourteen months before the diagnosis was made of an advanced carcinoma of the cervix uteri.

In another patient an intrauterine radium application (3,600 mg. hr.) was done for endometrial hyperplasia eight months before the patient was seen at the American Oncologic Hospital with a Stage III cervical lesion!

Of incidental interest is one patient who, although she did not have previous pelvic surgery, had a hemorrhoidectomy six months before a Stage III carcinoma was diagnosed.

It is apparent that a very high percentage (20.8 per cent) of the patients had had previous pelvic surgery. Some of this surgery was ill-advised and obviously inadequate in patients in whom the diagnosis of carcinoma of the cervix must have been suspected. Some of the surgery was performed in patients in whom the diagnosis of carcinoma of the cervix was apparently not suspected.

Whenever any type of pelvic surgery is contemplated the possibility of carcinoma of the cervix must be kept in mind. It is a wise precaution to perform a diagnostic curettage and circular cervical biopsy[6] preliminary to almost every type of gynecologic surgery particularly when technical difficulty is anticipated in performing the complete operation. The curettage may give valuable information and the circular cervical biopsy, in addition to being informative, is an effective means of treating the diseased cervix. This plan may be utilized in the training of a hospital resident staff. Patients who are about to have rectal surgery should certainly have the benefit of thorough gynecologic examination prior to the operation.

Plan of Treatment

During the period 1929 to 1934 the plan* of treatment, in general was as follows:

An intrauterine application of radium was given first. The radium is contained in tubes of 50 mg. each. Each tube is 30 mm. long and 2.3 mm. in external diameter with a wall thickness of 0.5 mm. of platinum. The tubes were placed in tightly fitting brass capsules (1 mm. in wall thickness), and then covered with 1 mm. of soft rubber. In the majority of cases two 50 mg. capsules were placed in tandem formation in the uterus, sutured with chromic catgut to the cervix, and allowed to remain in place for ten to thirty-six hours (most often twenty-four to thirty-six hours), depending upon the age and condition of the patient. In all cases the bladder and rectum were each protected by two 2 mm. lead shields, each covered by 2 mm. of plastic composition rubber and molded to fit the anterior and posterior vaginal walls. The lead shields were separated by tightly packed gauze to give added distance.

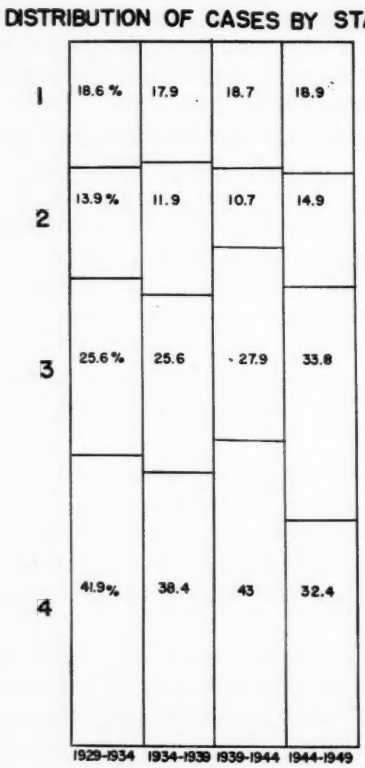

Fig. 2.

When the reaction had subsided, about three to six weeks following the application, another radium treatment was given. This time, the two 50 mg. tubes of radium were placed in the 1 mm. brass capsules and then covered together with a 1 mm. lead mold. This mold was then wrapped in a 1 cm. thickness of cotton gauze and the tubes were placed across the face of the cervix. The radium was allowed to remain in place about the same length of time and, as before, the bladder and rectum were each protected by 4 mm. of lead and 4 mm. of rubber.

*The method of treatment was originally devised by Dr. W. S. Newcomet and Dr. S. E. Tracy.

Following the second radium application the patients were given a course of deep roentgen therapy. The method of irradiation was as follows: Roentgen rays, generated at 200 kv., with a Thoraeus filter, were applied at a distance of 70 cm. (or a filter of 1 mm. of copper and 1 mm. of aluminum was used at a 50 cm. skin distance) to each of four pelvic portals, two anterior oblique and two posterior oblique. The size of the portals was usually 10 cm. by 10 cm. or 10 cm. by 12 cm.

Daily treatments of 300 to 600 r (measured in air) were used, alternating the fields so that a given area was exposed every fourth day. Each field received a dosage of from 1,600 to 1,800 r, the total dosage depending upon the rapidity with which the treatment was given and the general reaction of the patient to the irradiation.

During the period 1934 to 1939 the same general plan was followed but there was a tendency to increase the amount of irradiation so that 1,800 to 2,000 r was more often given.

In the years 1939 to 1944 the same general plan was followed, although there was some tendency toward an increased amount of x-irradiation.

During the time from 1934 to about 1940 a 4 Gm. radium bomb[7] was utilized. In a few of the cases, however, either because of untoward skin reactions to the roentgen radiation or when it was felt that the patient had received the utmost in roentgen therapy that was practical, the radium bomb was used to advantage.

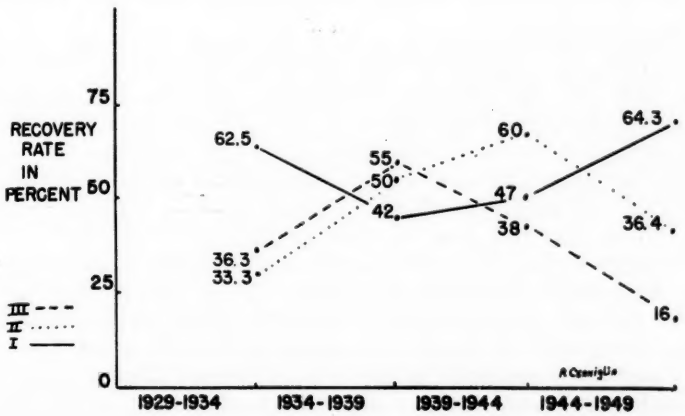

Fig. 3.—Five-year apparent recovery rate in different stages.

The amount of radium in the bomb was reduced to 1.5 Gm. in about 1940 and subsequently it was used less and less.

During the time 1944 to 1949 there was a gradual increase in the amount of external irradiation that was given so that the average patient usually received 2,100 r to each of four pelvic portals, with some patients receiving as much as 2,800 r to each of four pelvic portals. In addition, a changeover was made so that external irradiation was given preliminary to the radium applications. In certain selected cases vaginal cone therapy was also utilized. An attempt was made to devote more attention to individualization of cases so that interstitial radium was sometimes utilized and less reliance was placed upon the screening effect of the lead vaginal shields.

Results of Treatment

In Table I and Figs. 2 and 3, it is readily seen that the patients in the advanced stages (III and IV) outnumber the early-stage patients in a ratio

of almost two to one. This relationship has been almost constant since the original five-year period 1929 to 1934. In the matter of five-year survival the figures have not shown any definitive improvement and in the five-year period 1939 to 1944 there is a disparity in the results in that a better five-year survival rate resulted with the 10 Stage II cases than with the 17 Stage 1 cases. Whether this was just a chance occurrence or whether it was due to errors in original classification it is not possible to know at this time. Of the 288 patients who were treated, 76 have survived for a period of five or more years (26.3 per cent). Since 15 of these patients died because of intercurrent disease, the corrected survival rate is 27.8 per cent. Autopsies were performed on some of the patients. In the others the information was received from the physicians attending the patients at the time of their death and was believed to be correct.

TABLE I. NUMBER OF PATIENTS AND SURVIVAL BY STAGES

STAGE	PATIENTS TREATED		SURVIVAL	
	NUMBER	PER CENT	NUMBER	PER CENT
Stage I	53	18.4	28	52.8
Stage II	41	14.2	19	46.3
Stage III	82	28.4	29	35.3
Stage IV	112	38.8	0	0
Total	288		76*	26.3

*Fifteen died of intercurrent disease.

The 53 Stage I patients have a 52.8 per cent five-year survival, the 41 Stage II patients have a 46.3 per cent five-year survival, the 82 Stage III patients have a 35.3 per cent five-year survival, and the 112 Stage IV patients have the expected zero five-year survival rate. It is quite likely that the lack of improvement in the five-year survival rates has occurred because (1) there has not been a significant increase in percentage of Stage I patients who have been treated and because (2) there has not been a radical increase in the amount of radiation therapy that has been given.

In 1949 a supervoltage (1.75 megavolt) roentgen-ray machine was installed at the American Oncologic Hospital. By means of this machine it has been possible to deliver a tumor dose of 5,000 to 6,000 r without serious damage to the skin in a number of cases. Because of the demand for supervoltage therapy it has not been possible to use it as a planned method of treatment in all patients with carcinoma of the cervix. In the same year the radium at the Oncologic Hospital was divided into smaller units so that a greater flexibility in treatment might be employed. It is hoped that, with the greater stress[8] upon early diagnosis and more varied and exact methods of irradiation, with the judical use of indicated surgery, an increased survival rate will occur in those patients who are being treated at the present time.

Carcinoma of the Cervical Stump

The results of treatment in our patients with carcinoma of the cervical stump are summarized in Table II.

TABLE II. CARCINOMA OF THE CERVICAL STUMP

STAGE	TRUE	SURVIVAL	COINCIDENT	SURVIVAL
I	2	2	6	2
II	1	1	1	0
III	3	1	2	0
IV	7	0	6	0
		30.8%		13.3%

Twenty-eight of the 288 patients had carcinoma of the cervical stump, an incidence of 9.7 per cent. The age range was from 32 to 61 years, with an average age of 46.8 years. Six of the patients (21.4 per cent) were nulliparous, which corresponds closely to the figure of 22 per cent quoted by Redman.[9] He states that statistically 16 per cent of nulliparous women over the age of 34 have an intact uterus and the incidence of cervical carcinoma in this group is 4.7 per cent. He believes that nulliparity does not offer the same degree of protection against cervical carcinoma in the woman with the cervical stump as it does in the woman with an intact uterus.

Vaginal bleeding was the chief complaint in 22 of the patients, vaginal discharge was the most prominent symptom in 5 cases, and abdominal pain in one patient.

Fifteen of the patients had "coincident" carcinoma of the cervical stump. (A "coincident" carcinoma is one which occurs within two years of the original hysterectomy and is presumed to have been present at the time of the operation.) Only 2 of these patients, both Stage I cases, survived for a period of five years, 13.3 per cent.

There were 13 patients who had "true" carcinoma of the cervical stump. Three of these cases were detected within three years of the original operation, 2 were Stage IV, and one was Stage I. Four patients survived for five or more years, 30.8 per cent.

The total five-year survival rate for all the cervical stump patients was 6, or 21.4 per cent.

Seven of the patients had associated surgery at the time of the supravaginal hysterectomy. In the "coincident" group five had bilateral salpingo-oophorectomies, 3 in conjunction with a trachelectomy, and one patient had a trachelectomy without removal of the adnexa. One patient in the "true" group had removal of both adnexa. From this study it is not possible to make any statement in regard to the possible influence of the removal of the adnexa upon the subsequent course of the disease.

It seems reasonable to hope that carcinoma of the cervical stump should prove to be virtually nonexistent during the next decade or so. Most of the patients recorded undoubtedly had cancer present at the time of the supravaginal hysterectomy. The complete abdominal hysterectomy is in general a far wiser procedure to carry out and if it is necessary to allow the cervix to remain because of age or technical difficulties the cervix should certainly be treated by circular cervical biopsy and endocervical resection so that a histologic diagnosis is obtained and so that any abnormality of the remaining cervix is corrected.

Radiation Complications

There were 10 patients (3.5 per cent) who developed serious complications in association with their radiation treatment. One patient developed a large vesicovaginal fistula after she had been reirradiated because of a clinical diagnosis of bladder invasion without proof by biopsy. This patient subsequently had a bilateral cutaneous ureterostomy and is now living and well for over ten years. One patient had a colostomy performed because of radiation proctosigmoiditis, the colostomy was later closed, and five years later the patient has developed a rectovaginal fistula following ureteral surgery for an aberrant blood vessel at another institution.

Inflammatory reactions accounted for a high percentage of radiation complications. Two patients developed pelvic abscesses requiring drainage shortly after radium application, one patient developed an acute postradium salpingitis with a positive smear for the gonococcus organism, and one patient developed

a postradium ovarian abscess which required surgical intervention for diagnosis and treatment. One patient developed a generalized syphilitic rash after the institution of x-ray therapy and the treatments had to be discontinued for a while.

During an intrauterine radium application a uterus was perforated and required abdominal surgery for closure of the perforation and control of bleeding. This patient later received x-ray therapy and survived for more than five years.

Two patients died after having been treated with intrauterine radium. One patient developed auricular fibrillation which could not be controlled and the other patient developed a generalized peritonitis from which she never recovered.

All the complications occurred in patients who had been treated with radium as a preliminary to external x-irradiation. It is generally recognized that post-radiation inflammatory reactions will be less when x-irradiation is given prior to local radium therapy, but it is also understood that the trend toward greater amounts of irradiation will undoubtedly produce greater amounts of damage due to irradiation changes.

Fistulas

There were 14 patients who developed vesicovaginal fistulas due to carcinoma, 10 who developed rectovaginal fistulas due to carcinoma, and 6 patients who developed both rectovaginal and vesicovaginal fistulas prior to their deaths from carcinoma. One patient had a vesicovaginal fistula due to the trauma of childbirth and the 2 patients who developed fistulas associated with radiation therapy have previously been discussed.

Posttreatment Surgery

As shown in Table III, 36 patients had surgical procedures performed after their original treatment at the Oncologic Hospital. In 3 instances (the urethral plication, repair of vesicovaginal fistula, and the supravaginal hysterectomy) the operation was done for reasons not related to their malignant disease. The first two operations were performed to correct damage from childbirth trauma after it was considered that the cervical malignancy was under control. The supravaginal hysterectomy was done at another institution, in an advanced case. The reasons for the operative procedure are not clear.

TABLE III. POSTTREATMENT SURGERY, 36 CASES

Colostomy	10	Sympathectomy	1
Laparotomy (release of adhesions)	3	Salpingo-oophorectomy	2
Ureterostomy	1	Closure of perforation in uterus	1
Colostomy and ureterostomy of (1 adnectomy)	5	Colpotomy	2
Ligation of uterine vessels (1 with excision of rectal mass)	2	Urethral plication	1
Alcohol injections	5	Repair of vesicovaginal fistula	1
Nephrostomy	1	Supravaginal hysterectomy (elsewhere)	1

The remaining 33 patients (11.5 per cent) had surgical procedures which were related to their malignant disease.

There were 5 intraspinal alcohol injections and one sympathectomy for the relief of intractable pain. These procedures were all done in terminal patients and were reasonably successful.

The radiation complications requiring a colostomy, a bilateral cutaneous ureterostomy, closure of uterine perforation, colpotomies, and a unilateral salpingo-oophorectomy have previously been mentioned.

In addition, one patient required a unilateral salpingo-oophorectomy for the removal of a large benign ovarian cyst and one patient has recently been operated upon for the release of small-bowel adhesions which produced the symptoms and radiologic findings of a primary carcinoma of the small bowel.

There were 9 palliative colostomies done for the relief of bowel obstruction. One patient had a nephrostomy to overcome ureteral obstruction. There were 5 colostomies with associated bilateral ureterostomies in one of which an iliac lymphadenectomy was performed. There were two exploratory operations in which no definitive surgery was done. Two patients required abdominal surgery for the ligation of uterine vessels in order to control hemorrhage.

None of the patients upon whom palliative surgery was performed lived for longer than two years. One patient married after the performance of a colostomy and bilateral ureterostomy. The surgical procedures alone did not prolong life to any appreciable extent, but it was possible to reirradiate a number of patients with less difficulty and it is considered that a number of patients were made more comfortable by the procedures outlined.

Interesting Sites of Metastases and Causes of Death

It was not always possible in the instances of patients who did not die in the hospital to discover the ultimate cause of death aside from "carcinoma of the uterus."

The postirradiation causes of death have been mentioned earlier. One additional case might also be included in a nonmalignant category. This patient had repeated attacks of urinary infection following the completion of her irradiation therapy. The sulfonamide compounds were quite effective in controlling her urinary symptoms. She died elsewhere about three years after her original treatment. Complete autopsy revealed that death had been due to uremia due to sulfonamide crystals and there was no evidence of residual malignant pelvic disease.

Generalized metastases was listed most commonly as the ultimate cause of death. One of these patients had extensive metastases to the right side of the face and neck, another died with esophageal obstruction from metastatic spread, and another (previously reported[10]) exhibited the signs and symptoms of coronary disease due to metastases from carcinoma of the cervix uteri.

Henriksen[11] has emphasized the lymphatic spread of carcinoma of the cervix uteri and one must always be aware of the possibility of remote metastatic phenomena even when the local pelvic condition may clinically seem to be under control.

Summary

1. An evaluation and analysis of 319 patients seen and/or treated by irradiation for carcinoma of the cervix at the American Oncologic Hospital from Jan. 1, 1929, to Jan. 1, 1949, have been presented, with a follow-up of 95 per cent.

2. Race, age, and parity are discussed, with emphasis on the fact that 85 per cent were parous and 32.6 per cent were 40 years of age or younger.

3. Abnormal vaginal bleeding was by far the most prominent symptom.

4. Associated conditions, with 4.5 per cent positive Wassermann tests as the most common, were described.

5. Twenty and eight-tenths per cent of the patients had previous pelvic surgery. A plea is made for the more frequent use of a diagnostic curettage and circular cervical biopsy whenever pelvic surgery is done.

6. A description of the method of treatment is given with a five-year survival rate of 26.3 per cent for the 288 patients treated in the twenty-year period 1929 to 1949.

7. The results of treatment in 28 patients with carcinoma of the cervical stump (an incidence of 9.7 per cent) are noted. The importance of complete abdominal hysterectomy or other adequate treatment of the cervix is stressed.

8. The 3.5 per cent of cases in which serious postradiation complications developed have been described.

9. The 33 patients (11.5 per cent) who required posttreatment surgery are discussed and the palliative procedures are mentioned.

10. Interesting metastatic foci are mentioned and the possibility of remote metastases is emphasized even when there is no clinical evidence of local pelvic disease.

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DEVELOPMENT OF ENDOMETRIAL CARCINOMA SUBSEQUENT TO IRRADIATION FOR CARCINOMA OF THE CERVIX

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THE occurrence of multiple carcinomas of the uterus has been reported on many occasions.[1-7] Their diagnosis is usually made after hysterectomy has been done, and not prior to surgery.[1-4] The case here reported is especially interesting because of the development of adenocarcinoma of the endometrium fourteen years after the successful treatment of squamous-cell carcinoma of the cervix. A similar case was reported by Jacox, Major, and Baker,[5] in 1939 in which the original disease was carcinoma of the cervix. It was treated on three occasions over an eighteen-month period with interstitial radium; sixteen years later a diagnosis was made of adenocarcinoma of the uterus, squamous-cell carcinoma of the uterus, and fibrosarcoma of the uterus. The cervix was free of any demonstrable neoplastic changes at the time of hysterectomy. The main symptom during the interim was intermittent vaginal bleeding.

The present patient had a fourteen-year interval between the initial irradiation and the diagnosis of endometrial carcinoma.

Case History

L. M., a 62-year-old gravida i, para i, entered the hospital with the chief complaint of vaginal bleeding, which had occurred sporadically for thirteen years. She had been treated at another hospital with an unknown amount of intracavitary radium for carcinoma of the cervix in 1939. Prior to this therapy she had noted intermenstrual bleeding for an unrecalled period of time. No external therapy followed the intracavitary radium. Six months to a year after her therapy she began to have intermittent vaginal spotting and bleeding which occasionally simulated a menstrual period. During this thirteen-year interval she was seen by various physicians who ascribed this bleeding to "ovarian hypofunction." No biopsy or cytologic spreads were taken during this time.

Two months prior to admittance to University Hospital, the vaginal bleeding increased, and she consulted her family physician who referred her to another hospital for diagnostic curettage. The pathologist reported that the curettings contained well-differentiated adenocarcinoma of the endometrium. The patient was then referred to the Gynecology Tumor Conference for definitive therapy.

Past History.—Until her radiation menopause in 1939, the patient had had a regular 30 day menstrual cycle lasting 3 to 4 days, with a normal amount of flow. Her general health had remained good. Significant diseases included typhoid fever at age 2 and "inflammatory rheumatism" at age 9, both without residual damage. She had always been extremely obese.

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Physical Examination.—The blood pressure was 154/108. She was a well-developed, obese white woman whose weight was 245 pounds, and whose height was 64 inches. The rest of the physical examination was not remarkable except for severe varicosities with hypostatic dermatitis. Upon pelvic examination there were found normal external genitals. In the vagina there was adhesive vaginitis with areas of punctate hemorrhage. The cervix was clean but slightly atrophic. Under anesthesia the uterus was found to be symmetrically enlarged to the size of a three months' pregnancy, and was freely movable.

Laboratory Data.—Periphal blood and urine examinations were within the limits of normal. The glucose tolerance test was normal. The serologic test for syphilis (VDRL) was positive in 8 dilutions.

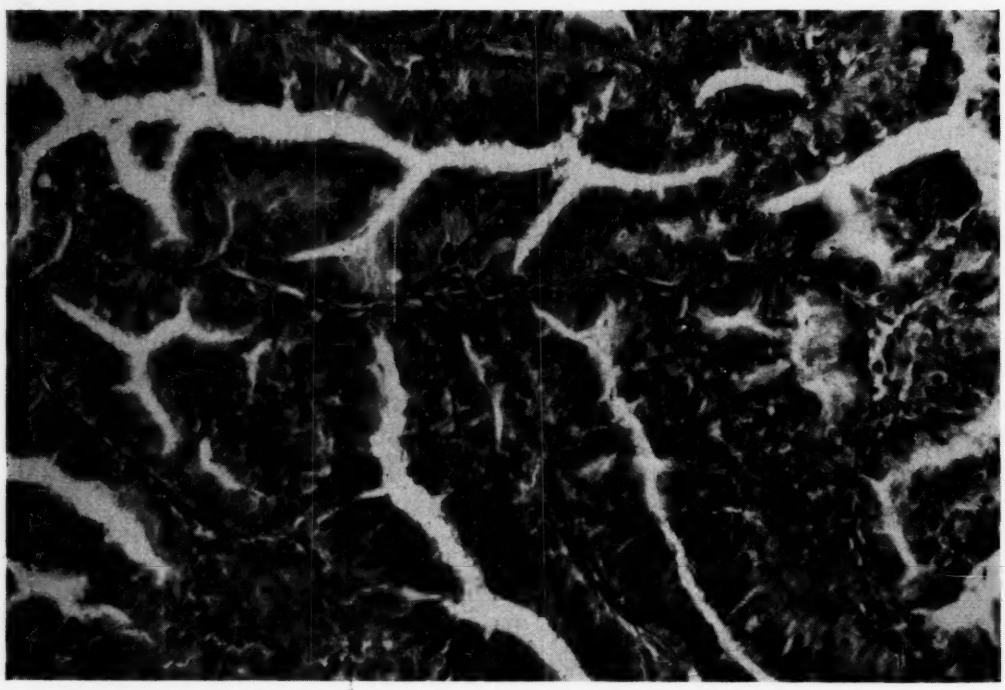

Fig. 1.—Photomicrograph of curettings in August, 1953, showing well-differentiated adenocarcinoma of the endometrium.

Hospital Course.—On Aug. 31, 1953, a dilatation and curettage and biopsy of the cervix were carried out. The uterus was sounded to 4 inches. The curettings were chunky, and grossly resembled carcinoma. Most of the tissue was located on the anterior wall of the uterus. The pathologic report on the specimens was: (1) well-differentiated adenocarcinoma of the endometrium (Fig. 1), (2) cystic hyperplasia of the endometrium, and (3) normal cervix. A 6 cm. tandem and 3 cm. colpostat filled with cobalt^{60} were inserted. The dose to the serosal surface of the uterus varied from 2,000 to 6,000 r. The endometrial surface dose was estimated to be 9,000 r. This cobalt application corresponds to a radium application of 3,780 mg. hr.

Six weeks later, total hysterectomy and bilateral salpingo-oophorectomy were done. The patient withstood the procedure well, and made an uneventful recovery. The summary of the pathologic report of the surgical specimen was as follows: The specimen consisted of a uterus, both tubes, and ovaries (Fig. 2). The uterus measured 10 cm. from cervix to fundus and 6 cm. between tubal insertions. The endocervical canal showed superficial necrosis of the endometrium. The fundus contained several polyps, the largest measured 1 by 0.4 cm. Microscopic examination showed (1) endometrial polyps, with adjacent endometrium showing little radiation effect, in other areas the endometrium being

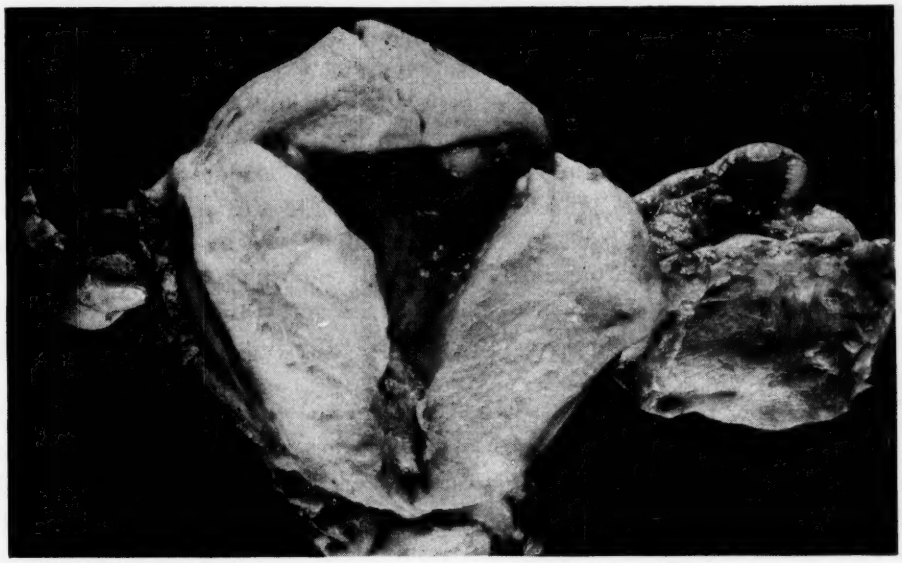

Fig. 2.—Photograph of gross specimen, October, 1953, showing uterus, tubes, and ovaries.

completely destroyed and the subjacent tissue necrotic; (2) radiation necrosis of the cervix; (3) fibroleiomyomas of the uterus.

The original slides of the cervical biopsy in 1939 were obtained and the diagnosis of squamous-cell carcinoma of the cervix was confirmed by our gynecologic tumor pathologist (Fig. 3). No mention was made as to the stage of the carcinoma of the cervix in 1939 (we know it was at least a League of Nations Stage I).

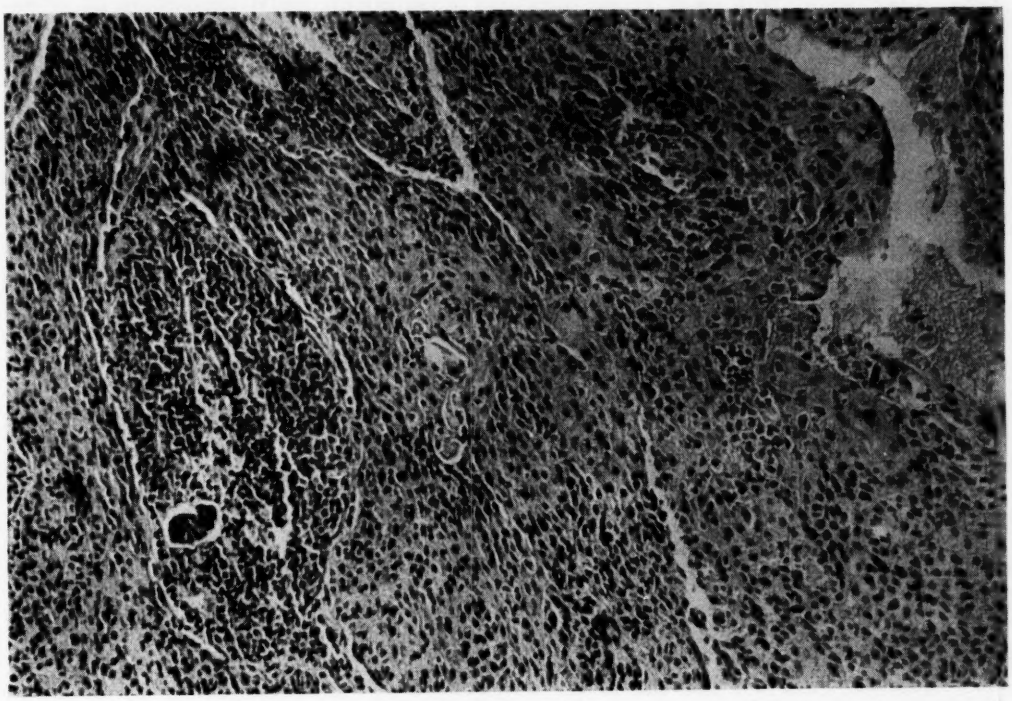

Fig. 3.—Photomicrograph of the biopsy specimen from the cervix in 1939, showing squamous-cell carcinoma.

Comment

Several interesting ramifications stem from this and similar cases. The first is the occurrence of multiple neoplasms. Counseller and Butsch[3] feel that the occurrence of multiple neoplasms in the same organ is more rare than in different organs, with the exception of the skin. Mider, Schilling, Donovan and Rendall,[8] in a recent statistical analysis, state that the patient who has been successfully treated for a specific anatomical type of cancer has the same probability as a noncancerous individual of developing another cancer. They do not mention those patients who have been successfully treated for cervical carcinoma with irradiation who subsequently develop carcinoma or sarcoma of the corpus.

The primary point of interest in this case, however, is the occurrence of endometrial carcinoma after the use of irradiation. The possibility of irradiation being a factor in the pathogenesis of carcinoma of the endometrium is favored by some. Lorenz, Eschenbrenner, Heston, and Deringer[9] demonstrated experimentally in rabbits that irradiation could produce carcinoma of the uterus. Speert and Peightal[10] pointed out that 8 per cent of their patients with malignant tumors of the uterus had had irradiation on an average of 8.3 years prior to the development of the malignancy. Hertig and Sommers,[11] in their well-documented "Genesis of Endometrial Carcinoma," feel very strongly that there is a definite correlation between the occurrence of corpus carcinoma and previous irradiation. The time interval in their cases was five to eight years between irradiation and the development of carcinoma. The time interval in this case from previous irradiation until diagnosis of endometrial carcinoma was made was fourteen years. Hertig and associates also state that endometrial polyps and cystic hyperplasia precede the development of carcinoma by a number of years. This patient had both cystic hyperplasia and endometrial polyps present when the diagnosis of endometrial carcinoma was made. Corscaden and Gusberg[12, 13] also support this viewpoint and found that irradiation for menopausal bleeding was followed by corpus carcinoma three and one-half times as commonly as is seen in the general population. They also suggest that statistically it occurs more frequently in the obese patient. This patient weighed 245 pounds.

Summary

1. A case is presented in which endometrial carcinoma developed fourteen years subsequently to irradiation for carcinoma of the cervix.

2. Multiple neoplasms are briefly discussed.

3. Points in favor of irradiation as a factor in the pathogenesis of endometrial carcinoma are enumerated.

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ENDOMETRIAL CARCINOMA AFTER BILATERAL OOPHORECTOMY*

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THIS presentation is based on a study of 130 cases in which bilateral oophorectomy had been performed without removal of the uterus. Our original object was to learn what happened to patients after bilateral ovarian ablation without removal of the uterus and also to establish criteria for the removal or retention of a uterus when a bilateral oophorectomy is performed. No published work has been found that may be used as a guide for either procedure.

In our investigation, however, we found 19 cases of uterine carcinoma, 8 of which were endometrial carcinoma which occurred after bilateral oophorectomy. This is exceedingly important, as many studies have implicated estrogen and the ovaries as probably causative of corpus carcinoma. It was decided, therefore, that this study should be devoted to the problem of endometrial carcinoma following bilateral oophorectomy.

Total Clinical Material

Data are presented first in Tables I and II on all 130 cases in which bilateral oophorectomy was performed but the uterus retained. This information constitutes the basis of our discussion of endometrial carcinoma.

TABLE I. SEQUELAE IN 130 CASES OF BILATERAL OOPHORECTOMY WITH THE UTERUS PRESERVED

Endometrial carcinoma developed in 8 cases
Cervical carcinoma developed in 11 cases
Intestinal obstruction developed in 3 cases
Benign lesions (fibroids) developed in 3 cases
No sequelae were recorded in 105 cases

TABLE II. DATA ON 105 CASES IN WHICH NO SEQUELAE ARE ON RECORD

51 cases were definitely checked and showed no sequelae
33 cases up to 5 years after salpingo-oophorectomy
18 cases more than 5 years after salpingo-oophorectomy
54 cases were not checked because
12 died from ovarian carcinoma or breast carcinoma
42 could not be traced

The occurrence of 3 cases of intestinal obstruction and 3 cases of myomas (Table I) after bilateral oophorectomy without removal of uterus is not significant except for the fact that the fibroids occurred or at least grew without the presence of ovaries.

Of the cervical carcinomas (Table I) the average time between the bilateral oophorectomy and the discovery of cervical carcinoma was 13.7 years.

*Presented at a meeting of the Obstetrical Society of Philadelphia, Dec. 3, 1953.

Young, Hertig, and Armstrong[1] found the latent period between the occurrence of cervical carcinoma in situ and clinically evident carcinoma to be 9 years. These findings are mentioned because they afford a comparison with similar data on endometrial carcinoma. Further than this, cervical carcinoma will not be discussed in this paper because it is well established that this occurs regardless of ovarian status.

Ages of Patients.—

The only interesting commentary on the ages of the patients (Table III) is that approximately half of them were in the childbearing age, and the remainder were past the menopause at the time of bilateral oophorectomy.

The patients who developed carcinoma of the uterus after oophorectomy are in the same age group as the carcinoma patients reported generally, regardless of the presence or absence of ovaries. This is significant in so far as ovarian relationship to endometrial carcinoma is concerned; it will be discussed fully in the latter part of this paper.

TABLE III. AGE AT TIME OF BILATERAL SALPINGO-OOPHORECTOMY

AGE (YEARS)	NO. OF CASES
19	1
20-30	26
31-40	34
41-50	37
51-60	20
61-70	10
71-80	2
Total	130

Indications for Original Operation.—

As shown in Table IV, bilateral oophorectomy with retention of the uterus was performed on 43 patients with benign cysts; most of these patients were in the childbearing age and a desire to limit surgery may have been the reason for leaving the uterus. Perhaps some surgeons have had Thorek's[2] dictum in mind, which was to leave the uterus intact when both ovaries were ablated, so that the patient would not consider herself entirely unsexed. There were 28 cases of malignant ovarian tumors; here the hopeless outlook for the patient may have influenced the operator to leave the uterus behind. There were 23 cases of pelvic inflammatory disease in which removal of the uterus may have been technically difficult and therefore inadvisable. There were 12 patients with normal ovaries in whom bilateral oophorectomy was done with retention of the uterus; these were patients with carcinoma of the breast and removal of the ovaries was done as a prophylactic measure against metastasis.

TABLE IV. PATHOLOGY AT TIME OF BILATERAL SALPINGO-OOPHORECTOMY

	NO. OF CASES
Benign cysts	43
Malignant ovarian tumors	28
Pelvic inflammatory disease	23
Normal ovaries	12
Endometriosis	9
Fibroma of the ovary	4
Atrophic ovaries	2
Granulosa-cell tumor	1
Tuberculous salpingitis	1
Hemorrhage	1
Pain	1
Actinomycosis	1
Unknown	4

Subsequent Development of Endometrial Carcinoma

We found 8 endometrial carcinomas in 130 patients who previously had had a bilateral oophorectomy, an incidence of 6.1 per cent (Table V). The incidence of corpus carcinoma in all women is about 1 per cent.

We must not, however, conclude from this that endometrial carcinoma occurs more frequently in castrated women than in noncastrated women. Because of the paucity of cases of bilateral oophorectomy with retention of the uterus it was necessary to collect cases from several sources. We were not always able to start our study with a patient at the time of the oophorectomy. We examined in addition many files of cases of uterine malignancy and those in which the ovaries had previously been removed were incorporated in our study. The incidence of sequelae as presented in this paper, therefore, is not a true percentage, first, because of our method of approach, and, second, because the number of cases is too small. All we can say is that in our study we found 8 cases* of endometrial carcinoma in patients whose ovaries had previously been removed.

TABLE V. CASES OF ENDOMETRIAL CARCINOMA

		AT TIME OF SALPINGO-OOPHORECTOMY			AT TIME CARCINOMA FOUND		
NO.	NAME	AGE	DATE	PATHOLOGY	AGE	DATE	YEARS AFTER SALPINGO-OOPHORECTOMY
1	C. H.	55	1947	Bilateral cystadenocarcinoma	61	1953	6
2	M. H.	47	1939	Cysts of ovaries	60	1952	13
3	I. B.	37	1924	Cysts	63	1950	26
4		45	1948	Carcinoma of ovaries	50	1953	5
5	C. L.	42	1946	Cystic ovaries	47	1951	5
6	M. H.	44	1931	Pelvic inflammatory disease	60	1947	16
7	P. W.	39	1942	Cysts of ovary	44	1947	5
8	N. B.	41	1942	Pelvic inflammatory disease	50	1951	9
9	L. G.	38	1924	Cystic ovaries and pelvic inflammatory disease	68	1954	30
	Average	43.7 years			54.3 years		10.6 years

In reporting the cases in which carcinoma was found we are not unmindful of the slow nature of the growth. According to Hertig and Sommers[3] carcinoma of the endometrium may become evident approximately 10 to 13 years after its inception.

Of the 8 patients with endometrial carcinoma in our series (Table V) the average age at the time of the bilateral oophorectomy was 43.7 years. The average age at the time that carcinoma was found was 54.3 years, so that the average time between the bilateral oophorectomy and the discovery of endometrial carcinoma was 10.6 years.

Two of the patients with endometrial carcinoma had previously had ovarian carcinoma. We therefore refer to Ryden's classification in order to make proper disposition of these two cases. Ryden[4] classifies cases of combined carcinoma of the fundus and ovaries into 3 groups: (1) carcinoma from the fundus to the ovaries, (2) carcinoma from the ovaries to the fundus, and (3) carcinoma of one ovary to another, and considers them metastatic if the second appears within 5 years; if beyond 5 years, they are classified as new

*Case 9 in Table V is an additional case found subsequently to the presentation of this paper.

primary lesions. As shown in Table V, both of our cases of endometrial carcinoma developed more than 5 years after bilateral oophorectomy for ovarian carcinoma.

We have investigated the literature in an effort to understand the possible etiology of endometrial carcinoma, with its relationship to the estrogens to hyperplasia of the endometrium, and to the ovaries. We believe that the opinions expressed by the authors are important enough to give at least a brief description of their studies. For clarification we have divided the literature into two sections, the papers that treat of estrogens and hyperplasia of the endometrium, and those concerned with ovarian factors.

Review of Literature

Fundus.—

The authors who believe that estrogen, which undoubtedly causes hyperplasia, is somehow a factor in the formation of carcinoma are:

Fremont-Smith and Vass[5] reported carcinoma following estrogen therapy.

Rigo and associates[6] found carcinoma in 8 of 546 women with glandular cystic hyperplasia. In the follow-up of 140 of these patients, 11 later developed carcinoma. It was concluded that this high incidence indicates a predisposition to carcinoma evidenced by glandular cystic hyperplasia; the agent responsible was believed to be estrogen.

Hertig and Sommers[3] presented circumstantial evidence which suggests the etiological importance of estrogen in endometrial hyperplasia caused by prolonged estrogen stimulation and they inferred that hyperplasia may be a forerunner of endometrial carcinoma.

Novak[8] said in 1947 that there is no proof that endometrial carcinoma arises from estrogen though hyperplasia is common and this may be related to carcinoma. Novak and Mohler[7] in 1953, however, felt that estrogen is implicated.

Tannhauser[9] stated that endometrial carcinoma is hormonal because uterine (myometrium and endometrium) activation is associated with *all* endometrial carcinomas (58 cases) and with only 23 per cent in nonmalignant uteri.

Speert[10] found that 4, or 33 per cent, of 12 patients with endometrial carcinoma had cirrhosis which was caused by failure of the liver to metabolize and convert estrogen to a less active form. This is 5½ times the usual incidence of cirrhosis in women over 40.

The following authors have the opposite opinion about estrogen as a cause of endometrial carcinoma.

Brewer and Foley[11] in a study of 34 women with endometrial carcinoma found no cirrhosis in any. Autopsies were performed on 144 women with cirrhosis; none had endometrial carcinoma, so the likelihood of estrogen as a cause of endometrial carcinoma is thus diminished, to a slight degree at least.

Emge[12] is vehement in insisting that there is no proved relationship between granulosa-cell tumors and carcinoma of the endometrium. Among 21 patients with granulosa-cell tumors and 8 with thecomas there was not a single carcinoma of the corpus, and endometrial hyperplasia was found in only 20 per cent. In data he obtained from 30 clinics a total of 514 granulosa-cell tumors was reported. In 17 there was co-existing endometrial carcinoma, an incidence of 3.3 per cent, in contrast to the 18 to 20 per cent reported by Hertig and 16 per cent by Dockerty. Conversely, in a collected series of 1,996 endometrial carcinomas there were only 7 cases of coexisting granulosa-cell tumors, an incidence of 0.35 per cent. Emge believes the occasional coexistence of granulosa-cell tumors and endometrial carcinoma does not indicate by any stretch of the imagination that estrogen imbalance is the cause of corpus carcinoma.

Pratt[13] reviewed 135 endometrial carcinomas, none with functioning ovarian tumors; he cited 5 cases of granulosa-cell tumors and endometrial carcinoma was not found in any. Most endometrial carcinomas occur after the menopause, so that the hormonal origin is not likely. He also stated that the extreme use of estrogen really has not produced carcinoma. Pratt suggested that heredity might be the cause.

Fahlund and Broders,[14] Jones and Brewer,[15] and Payne[16] stated that hyperplasia is seldom associated with carcinoma.

Engle and Smith[17, 18] and Hisaw[19, 20, 21] show that endometrial hyperplasia in the human being as a result of estrogen stimulation is at complete variance with the findings in monkeys.

Ovaries.—

In the study of the literature we find an almost equal division in the number of papers that purport to show that endometrial carcinoma is or is not caused by some ovarian factor.

In an attempt to correlate the findings and changes in the ovaries per se, studies of the structures of ovarian tissue under various conditions in association with carcinoma have been made. These studies have resulted in a substantial revision of the interpretation of the structure of the ovarian stroma long considered as consisting of connective tissue-like elements. Schwarz and Young[22] showed by histological studies that the cells of ovarian stroma, judging from their morphological and staining characteristics, have much more the properties of smooth muscle than of connective tissue. Di-Giorgi[23] stressed the structural similarity of the ovarian stroma to erectile tissue.

The following authors suggested that estrogen secreted by certain cells in the ovary may be a factor in the formation of endometrial carcinoma:

Shaw and Dastur[24] stated that certain peculiar cells, really an ovarian stromal-cell hyperplasia, were present in the hilus of menopausal ovaries in 24 of 48 cases of endometrial carcinoma. They suggested that these cells secrete a substance which causes the development of endometrial carcinoma. Of 9 patients with endocervical adenocarcinoma, such cells were present in 6, but in one patient with squamous-cell carcinoma they found no such cells. In 200 selected patients they found such cells in one, and this one patient was subsequently found to have had an endometrial carcinoma.

Woll and his associates[25] found stromal hyperplasia of the ovary in 56 to 92 per cent of carcinomatous uteri, and in only 36 to 42 per cent in a control group.

Novak[26] pointed to the possible influence of stromal (ovarian) hyperplasia on spontaneous postmenopausal hyperplasia; though there is no proof that endometrial carcinoma arises from estrogen, Novak stated that hyperplasia may be related to carcinoma.

Novak and Mohler[7] in a series of 63 cases of endometrial carcinoma found increased ovarian stromal-cell hyperplasia in 54 per cent, and in only 21 per cent of a control group.

The following authors also observed certain peculiar ovarian stromal cells, but did not believe they were factors in endometrial carcinoma:

Sternberg[27] reported cells similar to those observed by Shaw and Dastur[24] but in 80 per cent of 100 cases these cells appeared in normal ovaries from patients who did not have endometrial carcinoma.

Shillitoe[28] and Goldstein[29] both reported cells in normal ovaries of patients without endometrial carcinoma similar to those described previously.

Green and Peckham[30] presented data proving that such cells are not peculiar to the ovaries of patients with carcinoma; 63 of 127 patients showed these cells, 50 of these did not have carcinoma, 13 did.

Husslein[31] believed endocrinoid cells cause hyperplasia only; he found such hilus cells in 4 out of 5 cases of hyperplasia of the endometrium and concluded that they were found in cases of hyperplasia only. He studied 12 cases of uterine carcinoma with senile ovaries and found these cells in only one.

Further divergent viewpoints on the endometrial carcinoma-ovary relationship are those of:

Jones and Brewer[15] who stated that non-functioning ovaries do not prevent endometrial carcinoma. They stated that hyperestrinism or the unopposed action of estrin is not responsible for endometrial carcinoma.

Herrel,[32] who had never seen endometrial carcinoma in 241 cases in which oophorectomy had been previously performed.

Ingraham, Black, and Rutledge,[33] who stated that etiological factors within the ovary may be indicated because of (a) the frequency of endometrial carcinoma with granulosa-cell tumors and theca-cell tumors, (b) the spontaneous regression of the adenoma malignum type of endometrial hyperplasia following removal of granulosa-cell tumor, and (c) the apparent infrequency of endometrial carcinoma in surgical castrates.

From the evidence presented in the literature we note that many authors have endeavored to show that there is a close link to some endocrine disturbance in the causation of endometrial carcinoma. They discussed obesity, diabetic tendencies, liver cirrhosis with the failure of proper estrogen destruction. More specifically, they have presented evidence in support of the opinion that estrogen hormonal stimulation is a major factor in the causation of carcinoma of the uterus. Many authors point an accusing finger at the ovaries; one explanation agreed upon by many of the authors is that the ovarian follicle activity continues for variable lengths of time in nonovulating involutional ovaries and is perhaps responsible for postmenopausal endometrial hyperplasia as described by Novak and Yui.[34] The newer concept that the ovarian stroma with its peculiar stromal cells is causative of hyperplasia and even endometrial carcinoma has been advocated. Novak and Mohler[7] certainly look upon the ovary, the threadlike stromal cells in particular, as the source of the estrogen that is perhaps the inciting factor to fundal carcinoma in the predisposed postmenopausal patient; these cells might be the result of an abnormal stimulation of the pituitary gland, and this may be a result of a generalized metabolic or endocrine disturbance. Ingraham[33] stated that some clarification of the question of the relationship of the ovary to endometrial carcinoma could be made if authentic instances of carcinoma of the body of the uterus in surgically castrated women were available. Pemberton[35] stated that Smith[36] has reported 3 cases which occurred 15 years after total oophorectomy. Randall, Mirick, and Wieben[37] cited 4 such cases. Cases of carcinoma of the corpus in women rendered menopausal by irradiation have been recorded by Scheffey,[38] but it is evident from the report by Smith[39] that recrudescence of ovarian function may occur after heavy radiation. Roentgen ray or radium castration, therefore, cannot be taken as an absolute equivalent of surgical castration.

We have presented the pros and cons extracted from the literature. In spite of all this evidence and our own study we agree with Ingraham,[33] among others, that the relationship of estrogen, hyperplasia, and endometrial carcinoma is still unanswered; we do believe, however, that there is sufficient evidence presented to show that the ovaries themselves need play no part in the formation of endometrial carcinoma.

Summary

Of the 130 cases of bilateral oophorectomy in which the uterus was not removed, there were 3 cases of subsequent obstruction, 3 cases of fibroids, and 19 cases of uterine carcinoma (11 cervical and 8 endometrial).

The literature on estrogen, hyperplasia, and carcinoma has been reviewed.

As Ingraham[33] intimated, a report such as ours of 8 endometrial carcinomas which occurred in castrated women, and 3 cases of Smith[36] and 4 of Randall, Mirick, and Wieben,[37] making 15 in all, are evidence that should help to clarify the question of the ovarian cause of endometrial carcinoma.

Conclusions

1. Endometrial carcinoma can occur in patients after removal of both ovaries.

2. From the viewpoint of the literature and our own observation, it is not tenable to explain endometrial carcinoma by some aberrant activity in the ovary.

3. The occurrence of 8 cases of endometrial carcinoma in patients who had previously had bilateral oophorectomy is factual evidence sufficient to warrant total hysterectomy when both ovaries must be removed.

We are indebted to the following for their assistance in obtaining cases for this study: Dr. S. Leon Israel, Southern Division of the Einstein Medical Center; Miss Etta Jones, Pelvic Cancer Committee of the Philadelphia County Medical Society; Dr. Robert A. Kimbrough, Pennsylvania Hospital and Graduate Hospital; Dr. Charles Mazer, St. Agnes Hospital; Dr. Newlin F. Paxson, Hahnemann Hospital; Dr. Mary DeWitt Pettit, Woman's College Hospital; Dr. J. Robert Willson, Temple University Hospital.

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Discussion

DR. A. REYNOLDS CRANE.—This study by Dr. Cianfrani in effect says that the ovary is not necessary for the development of carcinoma of the uterus. In the light of our knowledge of the many factors which influence both normal and abnormal growth we can well agree with this conclusion.

The eight cases of fundal carcinoma are acceptable as such although one might question the two cases that developed following adenocarcinoma of the ovaries and one would like to know more about the nature of the lesions in the "cystic ovaries." A major problem is the latent period in the genesis of carcinoma. You are all familiar with the papers of Hertig, Speert, and Te Linde and his group, reporting endometrial abnormalities antedating fundal carcinoma by twenty years or more. At what stage do cell abnormalities preceding cancer become irreversible? Did these women have endometrial changes of an irreversible type when the oophorectomies were done? I would like to ask Dr. Cianfrani if he had an opportunity to study the endometria of any of these people at an earlier era, for this can be of significance in relation to the role of estrogens in fundal carcinoma.

The experimental work on mice in relation to estrogens and tumors is of great interest even if not directly applicable to man. Tumors of the breast in mice are sex linked, occurring in the female and with, as you know, a very high incidence in some strains. This incidence can be increased by reproductive activity and decreased by castration. Lacassagne produced tumors in male mice from susceptible strains by injection of estrogens. Subsequently the milk factor, a self-propagating substance similar to a virus, cold resistant, thermolabile, active in a broad alkaline pH range, separable by ultra centrifugation and chemical methods, etc., was shown by Bittner to be equally important. Newborn mice of tumor strains suckled by nontumor-strain mothers do not develop tumors nor do their descendants. Similarly, the incidence of tumors in a nontumor strain can be increased by suckling by tumor-strain mothers. In each instance, further variation can be induced by castration and reproductivity or tumors induced in males by combination of the milk factor and estrogens. The interaction of factors in carcinogenesis was also well shown by Bielschowsky who produced carcinoma of the thyroid in rats fed 2-acetoaminopyrine and thiouracil but not with the carcinogen alone without thiouracil.

Another observation pertinent to the subject animal is that of the strain of mice which after castration develop adrenal cortical hyperplasia, as a compensation of the castrate state. Does this ever happen in the human being? Present evidence indicates an increase in gonadotrophins but decrease in estrogens after the menopause, but there are still wide gaps in our knowledge of time relationships, ages, etc. How much variation in the metabolism of estrogen is there in different persons? Biskind showed that estrogen pellets planted in a spleen were ineffective in castrated animals on normal diets but were capable of sustaining estrus when the animals were rendered B deficient.

I have pointed out some of the complexities of carcinogenesis and would emphasize that, while estrogens are not per se capable of producing tumors, they do in some unknown fashion serve to influence the development of tumors especially at those sites normally subject to estrogenic stimulation.

DR. ROBERT A. KIMBROUGH, JR.—I would like to point out that Dr. Cianfrani does not maintain that his material is unselected. He has found 130 patients who had previously had a bilateral oophorectomy. One portion of his material was obtained by going through hospital records to locate such patients. The other portion of his material was obtained by going to the files of the Pelvic Cancer Committee and finding there those women who had already developed cancers who had previously had bilateral oophorectomy. Because this is not an unselected material, we cannot say that 8 of 130 women having this operation will develop endometrial malignancy nor can we say that 11 per cent will develop other forms of cancer.

DR. CHARLES MAZER.—Dr. Cianfrani's statistics bring out two valuable points: (1) that the uterus is not immune to the development of cancer after removal of the ovaries; (2) that estrogen, produced by ovaries, does not play a role in initiating the development of uterine cancer. Uterine cancer occurs at an age when the ovaries are functioning only slightly. Dr. Israel and I have assayed the blood and urine of castrates. The amount of adrenal estrogen found in the urine was negligible. None was demonstrable in the blood by the methods at our disposal.

I am convinced, as a result of experimental and clinical observations, that estrogens play no role in initiating the development of cancer. Estrogen does, however, accelerate the growth of existing cancer of the breast and uterus, just as it accelerates the growth of existing fibroids, but it does not initiate the development of the fibroids.

DR. S. LEON ISRAEL.—Dr. Cianfrani's diligent work, in addition to providing important factual information, has raised two interesting ghosts.

One of the ghosts has been well laid by Drs. Crane and Mazer, whose discussions clearly emphasized that estrogen is a tremendous stimulant to growth of organs which happen to have a high incidence of cancer and, in being such a stimulant, estrogen must of necessity be regarded as a secondary carcinogenic agent. It is one thing, however, to acknowledge that estrogen is a powerful growth hormone and quite another to interpret from the literature of cancer research that it is carcinogenic in women.

The second ghost, more fascinating because it is not too current in our thoughts, is the subject of uterine hormones. About 1906, Blair Bell described "uterin," the uterine hormone which he thought could be responsible for ovulation. Moreover, as late as seven years ago, reputable endocrinologists attempted to prove that the uterus produces a substance which acts as an ovarian stimulant. If "uterin" existed and if it had hormonal properties other than to induce ovarian function, there would be some rationale to permitting the uterus to remain behind in some instances of bilateral oophorectomy. Unhappily, there is no support for such a belief.

DR. CIANFRANI (Closing).—As to Dr. Crane's reference to the two patients with carcinoma of the ovaries who developed endometrial carcinoma, I would like to say that the records of one of these cases shows that the ovaries had been removed during a general surgical operation and a specific notation was made that no metastases were noted anywhere.

Dr. Crane also stated that he wished the diagnosis of cystic ovaries had been more detailed, particularly in the two cases of cystic ovaries in which carcinoma of the endometrium occurred five years later. I might add that in one of these cases in which the ovarian cysts were reported as benign there were no papilliforous growths or excrescences; no dilatation and curettage was done at the time of bilateral oophorectomy. In the other case the cysts were reported as simply benign; a curettage was done immediately prior to this bilateral oophorectomy and the result was reported as negative for malignancy.

I wish to thank Dr. Kimbrough for emphasizing the fact that the incidence of endometrial carcinoma in patients without ovaries must not be misconstrued. I thought I had mentioned this clearly, but apparently I did not stress its importance sufficiently.

THE "CLEARING" TECHNIQUE AND ITS APPLICATION TO THE STUDY OF THE PARIETAL PELVIC LYMPH NODES

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RADICAL abdominal hysterectomy with pelvic lymph node dissection continues to be used extensively in the treatment of carcinoma of the cervix. Likewise, postirradiation pelvic lymphadenectomy, as proposed by Taussig,[5] is experiencing ever-increasing popularity and widespread use. Hence it has become of paramount importance for the gynecological pathologist to recognize grossly and study microscopically as many of the lymph nodes as is possible. By so doing he can adequately document the degree of distant dissemination of the disease, if any, in the case at hand, and add to the store of our knowledge of the pattern of anatomical spread of cervical cancer. But of more importance, he can evaluate the effects of the various types, methods of administration, and dosages of irradiation therapy offered. In such ways, the pathologist plays an integral part in the compilation of statistics, only by the study and interpretation of which, in the light of our present limited knowledge, can we ever hope finally to obtain the correct answers to the how's and why's of the best treatment of this disease.

The purpose of this brief paper is to bring to the attention of gynecological pathologists and of others interested in the problem a technique whereby the gross identification of the lymph nodes is, in our opinion, greatly facilitated.

Every pathologist is more than casually aware of the great difficulty and tedium involved in taking a large piece of fatty tissue and going through it, bit by bit, with forceps and scissors, meticulously picking out the nodes. By means of this process, he often recovers only the enlarged nodes and misses many of the smaller and minute nodes which he well knows are present, but which are so small that he cannot identify them. It must be reiterated here that just because a node is so small as to be missed grossly, it cannot be conclusively assumed to be free of metastatic carcinoma cells. In direct reference to this, in the case of the pelvic nodes, Meigs[3] states that his group is convinced that positive nodes cannot be ascertained merely by palpation, visualization, and gross inspection, and that the only proof that a node contains or is free of malignant cells lies in the microscopic examination. Likewise, Cherry, Glücksmann, Dearing, and Way,[2] in a detailed study of the pelvic nodes removed in the course of radical surgery for cervical carcinoma, found that although 76 per cent of the nodes not palpable at operation did not con-

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tain tumor, *24 per cent were positive.* It is therefore imperative to recover all the nodes, enlarged and small. Indeed, many of the large nodes are found to be enlarged not by metastatic carcinoma but only by the follicular and reticulum hyperplasia caused by accompanying infection, so often associated with the malignant lesion. In addition, hyperplastic nodes are particularly common in the pelvic, inguinal, and femoral chains, due to distant benign infectious processes in the lower extremities and external genitals.

The problem of removing nodes from large pieces of fatty tissue is still pre-eminently that of the general surgical pathologist. It is he who must determine the status of the axillary nodes following radical mastectomy for carcinoma of the mammary gland, the mesenteric nodes following resection of the bowel for carcinoma, the perigastric nodes following surgery for gastric carcinoma, and so forth. As mentioned previously, however, with the revival of radical surgery in the treatment of uterine cancer and of regional lymphadenectomy following irradiation of the cervix and parametrium, and of radical groin dissection as an integral part of the treatment of carcinoma of the vulva, the gynecological pathologist has of necessity joined his confreres in facing and being burdened with this problem.

The laboratory technique about to be described was originally devised by Dr. Robert S. Grinnell of the Department of Surgery of the Presbyterian Hospital, New York City, as a diagnostic implement in his painstaking study of the metastatic spread of carcinoma of the bowel. It has been slightly modified and used extensively in the Department of Surgical Pathology of the Presbyterian Hospital in the study of carcinoma of the breast. To the best of our knowledge, however, this method has never previously been adapted on a large scale to the study of gynecological specimens, and, for this reason, we offer it as an implement for use by the gynecological pathologists.

The author has recently been associated with the Department of Pathology of the Francis Delafield Hospital in New York City. At this institution, there is no separate Gynecological Pathology Department and all surgical specimens are handled by the one laboratory. It was during the course of his work in this laboratory that the author first saw this technique employed in the study of appropriate gynecological specimens. He has since that time introduced it into the laboratories of the Sloane Hospital for Women of the Columbia-Presbyterian Medical Center, where, with abundant material, it is his intent to study the pelvic node-bearing tissue on a large scale.

"Clearing" Technique

The technique is very simple. It consists in treating the specimen, the iliac fat, with but four common chemical agents: formaldehyde, 95 per cent alcohol, absolute alcohol, and xylene. By means of these treatments, described in detail below, the fat is dissolved out almost in its entirety, leaving only translucent fibrous connective tissue, blood vessels, and the nodes. In other words, the specimen is "cleared of fat," hence the term "clearing" technique is used.

The lymphadenectomy is performed either via a transperitoneal or a retroperitoneal (extraperitoneal) approach. It is not in the domain of this article

to describe the technical steps of either of these procedures. Such descriptions may be found elsewhere in the literature (Brunschwig,[1] Twombly,[6] Taussig,[5] Nathanson[4]). One pertinent observation is salient at this time, however. If at all possible, it is greatly to be desired that the lymph node-bearing tissue be removed in one piece. This of course will depend on the skill of the operator, his intimate familiarity with the local anatomy involved, and the lack of such technical impediments as excessive scarring from previous surgical procedures, irradiation, or old infectious processes, obesity, improper hemostasis, inadequate exposure, and so forth. But by so removing the iliac fat

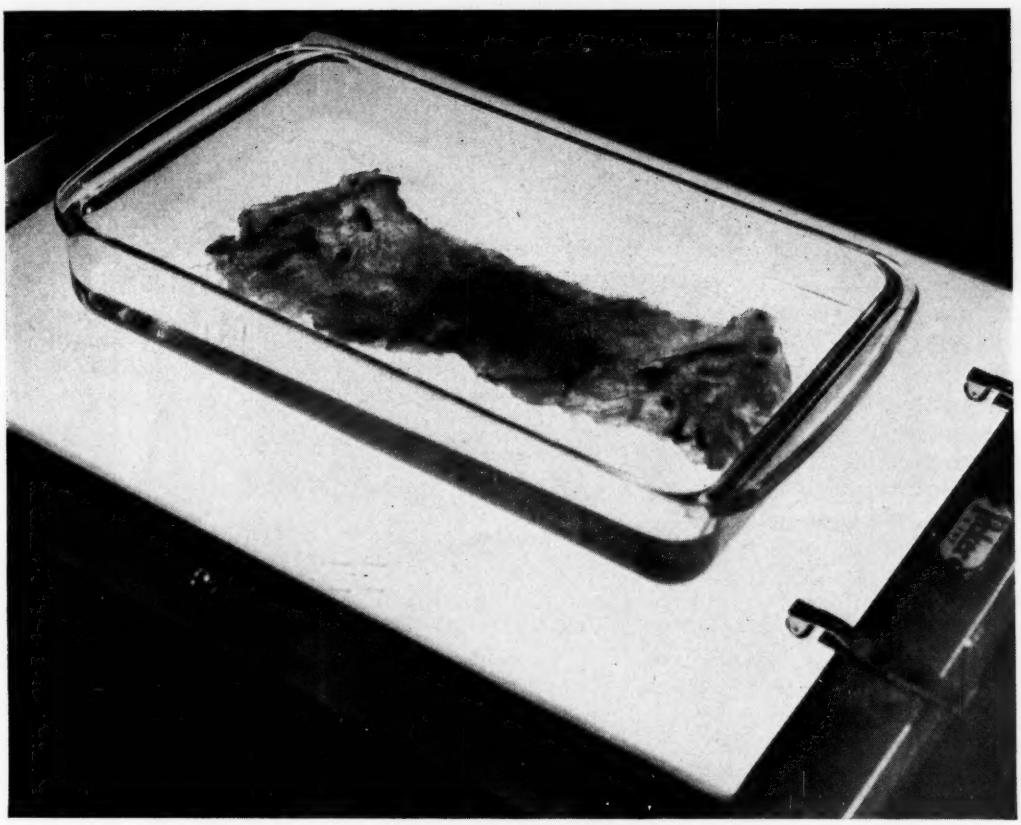

Fig. 1.—Ready to pick the nodes. The specimen lies in a flat dish, covered with xylene, over a source of bright light.

in one piece, the operator, by means of appropriate identifying methods (ties, clips, clamps, etc.), can orient the pathologist as to which part of the specimen represents the hypogastric tissue, which the tissue from the obturator fossa, and so on. Obviously, such identification can be made even if the tissue is, of necessity, removed piece by piece, but this usually entails confusion and resulting inaccuracy. A second reason for exerting a real effort to remove the fatty tissue en bloc is that it in many ways facilitates the carrying out of the "clearing" process. And, third, it is the opinion of the author, who has some familiarity with the surgical steps involved, that an effort to remove the tissue in toto probably results in a more complete extirpation of the node-bearing tissue than if it be removed piecemeal. But whether in toto or piecemeal, proper identification and orientation are absolutely necessary and must

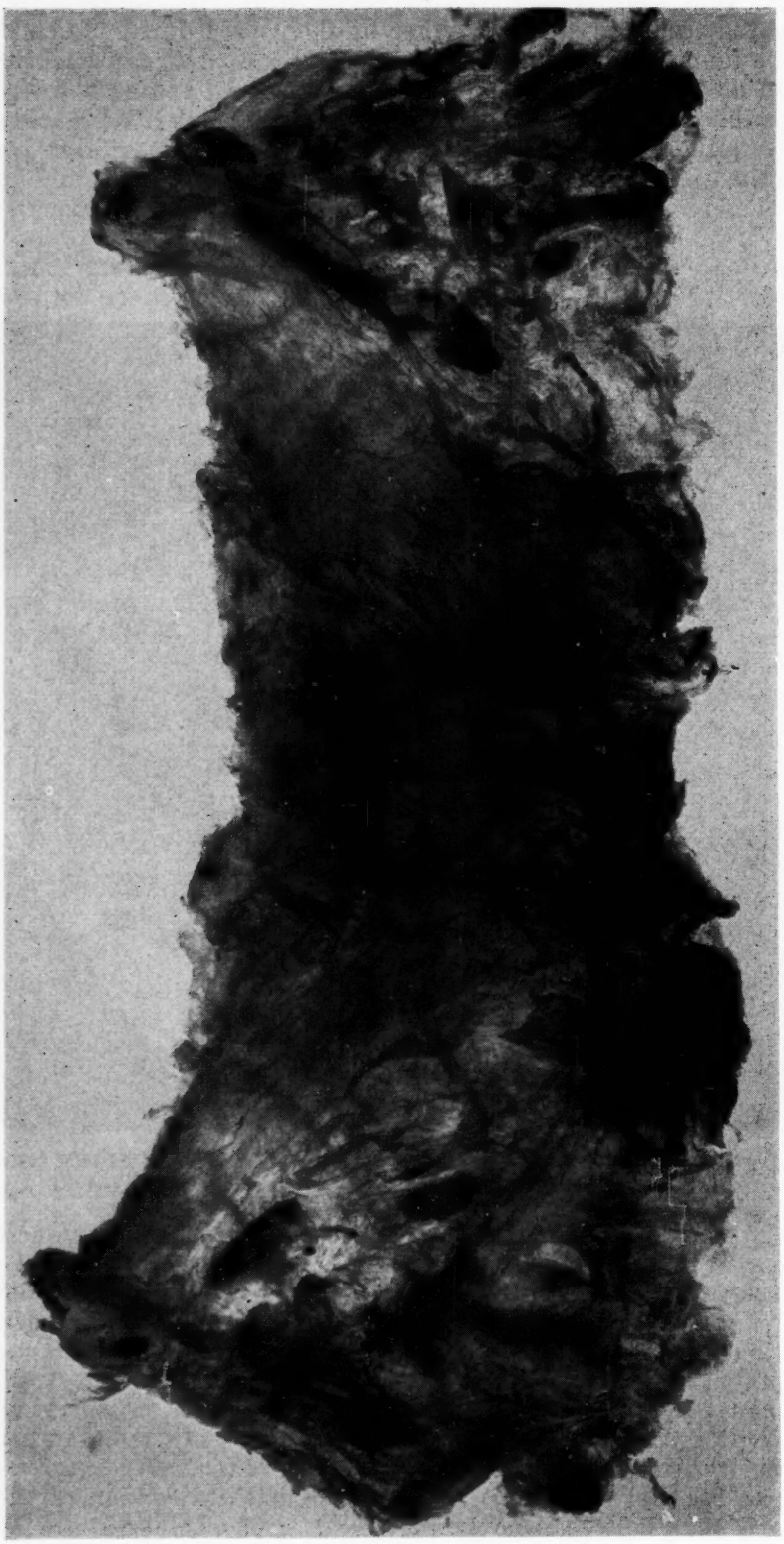

Fig. 2.—A "cleared" specimen for demonstration purposes from the Department of Pathology, Francis Delafield Hospital. The nodes appear as discrete, homogeneously dark, round, oval, and elongated masses.

be stressed. Nothing is more confusing, frustrating, and utterly useless in the over-all study than a positive node here, a positive node there, several negative nodes, and a group of positive nodes somewhere else.

Once removed from the body, the specimen is kept moist in saline-soaked gauze until it reaches the laboratory. It is not immediately fixed. Once arrived in the laboratory, the entire specimen is gently washed in running tap water to remove as much fresh and clotted blood as possible. The entire specimen is then completely immersed in a solution of nine parts 95 per cent alcohol and one part formaldehyde. We have been accustomed to using an ordinary Mason jar for the entire procedure, but any wide-mouthed vessel of adequate capacity would be suitable. The specimen, immersed in this solution, is incubated at approximately 60° C. for not less than twelve or more than twenty-four hours. At the end of this time, the specimen is removed from solution and kneaded or "worked" digitally to remove the absorbed solution and what fat has already been liquefied. This kneading should not be unduly rough for fear of traumatizing and fragmenting the nodes, but it can be performed with considerable vigor and digital pressure. This step can be carried out on a cutting board or any flat surface or in a flat dish. When the specimen is "worked" dry, it is immersed in a clean solution of 95 per cent alcohol alone and incubated at the above temperature for approximately one hour, following which it is kneaded once again, and re-treated with a second bath of 95 per cent alcohol for one hour. The specimen is again "worked" dry and incubated in absolute alcohol for one hour. It then is kneaded once again, and reimmersed for the last time in absolute alcohol, for one hour.

Following this fifth bath, the specimen is again kneaded dry, spread out in an ordinary flat Pyrex dish to approximate its original form and dimensions, and covered with a thin layer of xylene. The Pyrex dish is placed over a source of bright light, which we have found best and most easily supplied by an x-ray view box placed on its back (Fig. 1). The specimen, by this time, will be found to consist entirely of fibrous tissue, coursing through which the blood vessels will be prominent. The lymph nodes will appear as rounded or oval homogeneously dark varied-sized masses, usually in close proximity or apposition to the blood vessels (Fig. 2). They are now picked out with forceps with ease, placed in cassettes, again with proper identification, and turned over to the technicians for routine sections and special stains if so desired.

Several points must be stressed at this time. Before picking the nodes from the "cleared" specimen, we have made it a point to make a schematic diagram to describe the various chains in situ, and by so doing are able to correlate the microscopic findings with the actual anatomical pattern of the chains of nodes as they existed within the patient. Also, it is important that multiple blocks be made of the larger nodes. And, finally, it is recommended that the pathologist take for section even the most minute structures from the "cleared" specimens, if he is in any doubt of their being nodes or not. Granted, some sections will prove to be not lymphoid tissue at all but only thickened fibrous tissue or a small clot of blood or part of a small vessel, but often he will be rewarded for his diligence by being able to study small but definite nodes which otherwise would certainly have been missed.

In summary form, therefore:

1. The specimen is gently but thoroughly washed in running tap water.
2. The specimen, unfixed, is immersed and incubated at 60° C. in a solution of 9 parts 95 per cent alcohol and 1 part formaldehyde, for not less than 12 or more than 24 hours.

TABLE I. A COMPARISON BETWEEN THE NUMBER OF NODES RECOVERED FROM "NOT CLEARED" AND "CLEARED" SPECIMENS

NAME	OPERATION	SIDE	EXT. ILIAC	HYPOGASTRIC	OBTURATOR	OTHERS	TOTAL
Not Cleared.—							
A. G.	Post-irrad. lymphadenectomy	Right	----------	"Several"	----------	--	"Several"
A. W.	Radical hysterectomy and lymphadenectomy	Bilateral	1 (left) 1 (right)	0 (left) 0 (right)	1 (left) 1 (right)	--	2 2 } 4
M. R.	Post-irrad. lymphadenectomy	Bilateral	0 (left) 1 (right)	1 (left) 1 (right)	3 (left) 4 (right)	--	4 6 } 10
E. H.	Radical hysterectomy and lymphadenectomy	Bilateral	2 (left) 2 (right)	0 (left) 0 (right)	0 (left) 0 (right)	"Ureteral" 2	2 2 2 } 6
A. F.	Radical hysterectomy and lymphadenectomy	Bilateral	0 (left) 0 (right)	2 (left) 3 (right)	3 (left) 3 (right)	--	5 6 } 11
J. B.	Colpectomy; radical hysterectomy and lymphadenectomy	Bilateral	1 (left) 1 (right)	1 (left) 1 (right)	0 (left) 5 (right)	--	2 7 } 9
R. S.	Radical hysterectomy and lymphadenectomy	Bilateral	0 (left) 0 (right)	0 (left) 1 (right)	2 (left) 1 (right)	--	2 2 } 4
S. W.	Radical hysterectomy and lymphadenectomy	Bilateral	"Several" (left) 0 (right)	"Several" (left) "Several" (right)	0 (left) 0 (right)	--	"Several"
M. J.	Post-irrad. lymphadenectomy	Bilateral	Nodes not identified			--	13
P. P.	Radical hysterectomy and lymphadenectomy	Bilateral	1 (left) 3 (right)	0 (left) 0 (right)	0 (left) 1 (right)	--	1 4 } 5
B. R.	Radical hysterectomy and lymphadenectomy	Bilateral	"6 nodes on left; 8 nodes on right"			--	6 8 } 14

Cleared.—									
A. G.		Post-irrad. lymphadenectomy	Left		Nodes not identified		--	9	
M. T.	1)	Post-irrad. lymphadenectomy (extraperitoneal)	Right	4	Continuation of operative procedure technically unsuccessful		--	4	12
M. T.	2)	Post-irrad. lymphadenectomy (transperitoneal)	Bilateral		Nodes not identified		--	8	
R. R.		Post-irrad. lymphadenectomy	Left	0	5	8		13	
C. S.		Radical hysterectomy and lymphadenectomy	Bilateral		Nodes not identified		--	24	
A. D.		Post-irrad. lymphadenectomy	Bilateral	6 (total)	7 (left) 4 (right)	0 (left) 0 (right)	--	7 6 4	17
R. B.		Radical hysterectomy and lymphadenectomy	Bilateral		Nodes not identified		--	20	
M. H.		Radical hysterectomy and lymphadenectomy	Bilateral	10 (left) 7 (right)	5 (left) 8 (right)	5 (left) 0 (right)	--	20 15	35
K. F.	1)	Post-irrad. lymphadenectomy	Left	6	4	2	--	12	30
K. F.	2)	Post-irrad. lymphadenectomy	Right	4	8	6	--	18	
K. R.		Hysterectomy and lymphadenectomy for endometrial carcinoma with secondary carcinoma in the cervix	Bilateral	9 (left) 9 (right)	5 (left) 14 (right)	2 (left) 0 (right)	--	16 23	39
I. B.	1)	Post-irrad. lymphadenectomy	Left	5	3	3	--	11	22
I. B.	2)	Post-irrad. lymphadenectomy	Right	6	5	0	--	11	
M. R.	1)	Post-irrad. lymphadenectomy	Left	8	4	2	--	14	24
M. R.	2)	Post-irrad. lymphadenectomy	Right	7	3	0	--	10	
N. P.	1)	Post-irrad. lymphadenectomy	Left	3	6	1	--	10	22
N. P.	2)	Post-irrad. lymphadenectomy	Right		Nodes not identified			12	

3. Knead or "work" dry by digital pressure and manipulation.
4. Immerse and incubate in solution of 95 per cent alcohol for 1 hour.
5. Knead.
6. Immerse and incubate in 95 per cent alcohol for 1 hour.
7. Knead.
8. Immerse and incubate in absolute alcohol for 1 hour.
9. Knead.
10. Immerse and incubate in absolute alcohol for 1 hour.
11. Knead.
12. Spread tissue in flat dish over a source of bright light, cover with xylene.
13. Diagram nodes in situ.
14. Pick nodes.

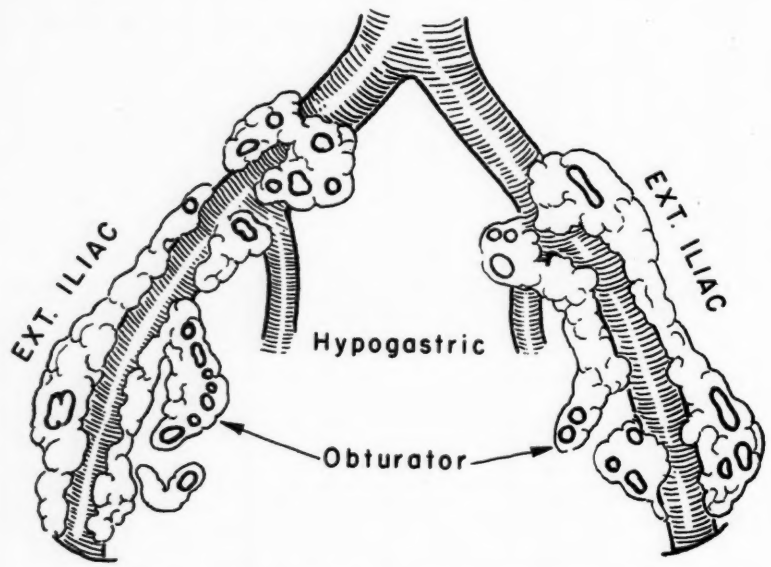

Fig. 3.—Case 2. Reconstruction of lymph node chains in situ about great vessels of the pelvis. Thirty nodes all negative for metastatic cancer.

Table I compares 17 cases in which the "clearing" process was used to identify the nodes with 11 cases in which the nodes were identified and picked without previous chemical removal of the fat. As can be seen from perusal of this table, the total number of nodes, when removed bilaterally, ranges between "several" and 14 or an average of slightly better than 8 nodes per case in the untreated specimens. In striking and statistically significant contrast, however, the total number of nodes, bilateral, recovered from the "cleared" specimens ranges between 12 and 39 nodes. An average of almost 25 nodes were recovered and microscopically studied per case, *three times* the number of nodes obtained by merely picking from the untreated surgical specimen. This great discrepancy in the numbers of nodes recovered and studied histologically affords ample evidence of the efficacy of the technique and its potential usefulness to the gynecologic pathologist.

Following are three representative gynecological cases in which we think that the "clearing" technique was of benefit in the study of the pathological specimens.

CASE 1.—Mrs. M. H. (No. 2293) was a 45-year-old Puerto Rican, para iv, gravida iv. In April, 1953, a radical abdominal hysterectomy, bilateral oophorectomy, and bilateral pelvic lymph node dissection were performed for epidermoid carcinoma of the cervix, Stage II. A total of *35 lymph nodes* were grossly identified following "clearing" of the iliac fat. Twenty nodes were recovered from the left side and 15 from the right lateral wall. All nodes were negative for metastatic carcinoma, and revealed only varying degrees of hyperplasia, fibrosis, and hemosiderosis.

CASE 2.—Mrs. K. F. (No. 1126), a 63-year-old para i, gravida i, Negro woman, had a diagnosis of epidermoid carcinoma of the cervix with a superficial granular extension along the left lateral wall to the upper segment of the lower third of the vagina. Therapy consisted of radium in tandem in the cervicouterine canal and in the vagina against the cervix, according to the Manchester technique, to deliver 6,000 r to Point A, followed by 4,000 r TD external x-ray on the 2 MV machine, through two opposing 15 by 15 cm. fields with a 3 cm. lead strip, in four weeks' time. She finally received intravaginal radium, in Manchester

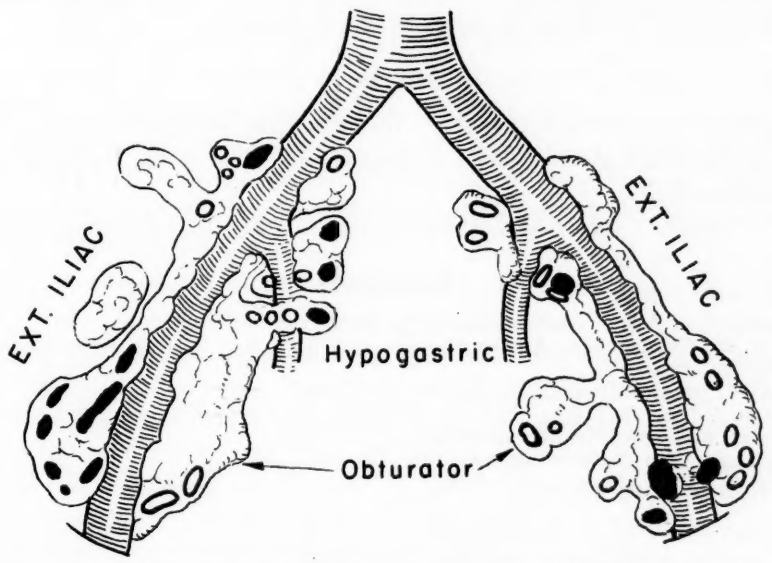

Fig. 4.—Case 3. Reconstruction of lymph nodes in situ. Thirty-nine nodes studied; 15 nodes positive for metastatic cancer. Blackened nodes are positive.

ovoids, so calculated as to deliver 4,000 r to the vaginal extension. In December, 1952, bilateral pelvic lymph node dissections were performed. *Twelve* lymph nodes were recovered from the "cleared" specimen from the left lateral pelvic wall. All nodes were negative for cancer, and revealed thickened capsules, extensive fibrosis, thick-walled blood vessels, and reticulum hyperplasia. *Eighteen* nodes were studied from the right iliac fat. These nodes all were free of malignant cells and showed a histological picture similar to that previously described (Fig. 3).

CASE 3.—Mrs. K. R. (No. 2506) was a 63-year-old white para iv, gravida iv. In January, 1953, a modified total hysterectomy, bilateral salpingo-oophorectomy, and bilateral pelvic lymph node dissection were performed for carcinoma of the endometrium with secondary carcinoma in the cervix. *Sixteen* lymph nodes were recovered from the fatty tissue from the left lateral pelvic wall after "clearing." Four of these nodes contained metastatic carcinoma. *Twenty-three* lymph nodes were recovered from the right iliac fat following "clearing," and 11 nodes contained carcinoma (Fig. 4).

Comment

The purpose of this paper has been to describe a laboratory technique which will prove of value in the concentrated study of gynecological specimens, admittedly of one limited sort, but probably one of the most important specimens with which the gynecological pathologist deals. No series of adequate size has been compiled to date, but such compilation is in progress, and when and if significant figures can be derived, such results will be subsequently reported.

If the element of speed is important, for any reason, then this technique is not adaptable in such cases. The very nature of the "clearing" technique adds some 48 to 72 hours to the over-all study, but we are convinced that thoroughness and minute detail must be the prime consideration to the absolute exclusion of haste.

The physical equipment for this technique is to be found in every laboratory. The element of added expense need not be great.

Summary

A method to facilitate the gross identification of lymph nodes from fatty tissue in gynecological specimens is presented. The need for such identification is discussed.

The "clearing" technique reveals a significantly higher number of nodes.

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MALIGNANT TRANSITION IN OVARIAN ENDOMETRIOSIS

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MANY gynecologists and pathologists have entertained the belief that endometriosis has as much capability of malignant change as does endometrium normally located. Examination of surgical and autopsy specimens frequently reveals the presence of ovarian endometrial cysts that have been asymptomatic. Could not, and do not, some of these areas of ectopic endometrium undergo malignant degeneration? The possibility seems reasonable but verification has been difficult to obtain. Many far-advanced carcinomas of the ovary, which may have originated in this ectopic tissue, have undoubtedly destroyed evidence of such origin.

Sampson,[6] one of the most widely known early protagonists of the malignant potentiality of endometriosis, stipulated certain rigid requirements for such a transition. First, there must be "actual demonstration of both cancerous and benign endometrial tissue in the same ovary." Second, the benign and malignant endometrial tissue must bear "the same histologic relation to each other that cancer of the body of the uterus bears to the nonmalignant portions of the endometrium of that uterus." He further insisted that "it must be shown that the cancer arose in this tissue and that it is not invading it from some other source." Additional supportive evidence is desirable and could include the presence of tissue similar to endometrial stroma enclosing distinctive epithelial glands, and the identification of old (not fresh) hemorrhage. It has also been stated[7] that, ideally, another condition might be imposed, namely, the demonstration of benign and malignant endometriosis adjacent to and in continuity with each other.

Adenoacanthomatous change in endometrial adenocarcinomas is being recognized with increasing frequency. It should not be too unreasonable to consider as persuasive evidence of malignant change of endometriosis the fact that adenoacanthomatous variations have occurred in ovarian adenocarcinoma. A recent report on primary adenoacanthomas of the ovary indicated that in probably three of five cases the malignancy arose from endometriosis.[2] Sampson's criteria, however, could not be met.

Scott[7] reported three cases, two of which had a probable origin in endometriosis and one which did so arise, and collected twelve additional instances from the literature in which Sampson's criteria had been fulfilled. Of these

cases, four[1, 3, 4, 5] showed adenoacanthomatous change. Adequate demonstration of malignant change in endometrial cysts of the ovary is thus unusual. The case to be reported here meets not only the conditions imposed by Sampson but also the condition considered by Scott as desirable.

Case Report

A 50-year-old white woman was admitted to the Millard Fillmore Hospital on Sept. 27, 1953, with the chief complaint of stress incontinence of about two years' duration, which had become much worse during the six months prior to hospital admission. She had no history of cystitis or of dysuria. There were no complaints referable to the rectum. She had had a normal delivery of a term pregnancy in 1930, and a cholecystectomy and an appendectomy were done in 1930. She had suffered a "sprained back" in 1951 with some intermittent discomfort since that time.

Upon physical examination the patient was found to be well-developed and well-nourished, and in no acute distress. The findings on physical examination were negative except for the presence of a reducible incisional hernia through a right rectus surgical scar, and a cystocele and rectocele. Results of laboratory studies were within normal ranges.

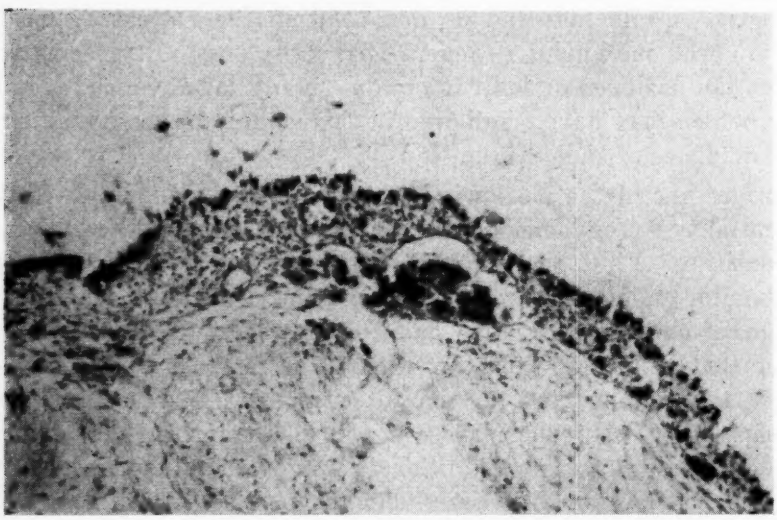

Fig. 1.—An area of the cyst wall is lined by typical endometrial columnar cells with an underlying zone of stromal cells and pigmented macrophages.

On the day after admission an anterior and posterior colporrhaphy was performed by Dr. Frederick G. Stoesser. Immediately thereafter the abdomen was entered through a Pfannenstiel incision and a tumor mass, about 15 cm. in diameter, was found. This was wedged firmly in the pelvis and was adherent to it posteriorly. Further examination revealed the tumor mass to be a right ovarian cyst with invasion of the right broad ligament and surrounding invasion of the right ureter. The cyst contained chocolate-colored fluid and bits of necrotic matter. A supravaginal hysterectomy with a bilateral salpingo-oophorectomy was therefore done.

Upon gross pathologic examination, the uterus, triangular in shape, measured 7 cm. vertically, 6 cm. across the fundus, and 3 cm. across the anteroposterior diameter. The myometrium was of uniform thickness and the endometrium was thin and slightly hemorrhagic. A soft polyp, 2 cm. long, arose from the endometrial surface. The Fallopian tubes were not remarkable. The left ovary was small and fibrotic. The right ovary consisted of a previously opened thick-walled cystic structure, which measured 7 cm. in

Fig. 2.—The point of malignant transition in the endometrial cyst. At the right is noted the flattened columnar epithelium and at the left the piled-up and atypical cells of the neoplasm can be seen.

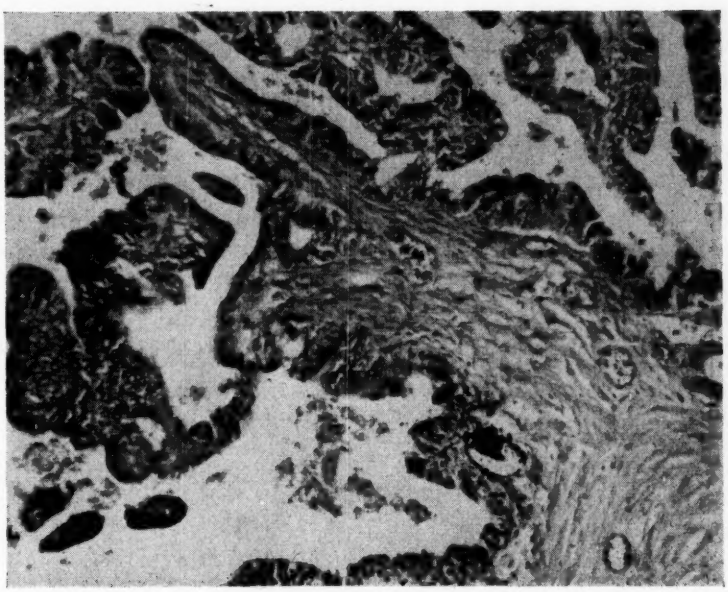

Fig. 3.—Section showing atypical neoplastic features of the tumor.

diameter in its partially collapsed state. The inner surface was covered by thick, dark-brown material, part of which could be wiped away. Arising from the wall of the cyst and infiltrating it were two nodular projections, 2 and 4 cm. in diameter, respectively. On section these were soft and contained some yellowish granular material.

Microscopically the endometrium of the uterus was atrophic as manifested by scattered, small, ovoid glands separated by a scant amount of stroma. The endometrial polyp was benign and was composed of cystically dilated glands. The myometrium and the Fallopian tubes were not abnormal.

Section of the left ovary showed a small endometrial cyst near the surface where there was puckering and adherent tabs of fat were found.

Multiple sections of the cystic right ovary (Figs. 1, 2, and 3) revealed the wall of the cyst to be composed of compressed ovarian stroma. The lining consisted of granulation tissue containing large pigmented histiocytes, and blended in adjacent areas with a layer of endometrial cuboidal cells which rested directly upon the underlying compressed ovarian stroma. In other portions the cuboidal cells were separated from the underlying ovary by a distinct zone of stromal-cell tissue which also contained scattered foci of pigmented macrophages.

At one point the endometrial lining cells of the cyst showed a malignant transition beyond which there was a papillary carcinoma which projected into the cyst and also showed downward growth into the ovarian stroma. The adenomatous pattern of the neoplasm was interrupted occasionally by squamous-cell replacement of the columnar cells. This was associated with keratohyaline production within the glands with occasional spillage of this substance into the surrounding ovarian stroma. In these areas multinucleated foreign-body giant cells surrounded the amorphous pink-staining "keratin-like" substance.

Summary

1. Thirteen cases of ovarian carcinoma considered as having met Sampson's conditions for proving an endometrial origin have been previously reported.

2. Of these cases, four showed adenoacanthomatous change.

3. A case is presented which is considered adequately to fulfill Sampson's criteria for an endometrial origin, making the fourteenth case reported to the present.

4. This case is the fifth reported instance, so far as can be ascertained, of ovarian adenoacanthoma known to arise from endometriosis.

5. In this case it was also possible to demonstrate benign and malignant endometriosis adjacent to and continuous with each other.

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VAGINAL SEQUELAE OF VAGINAL HYSTERECTOMY*

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VAGINAL hysterectomy is accompanied by less morbidity, causes less postoperative discomfort, and is somewhat less hazardous than abdominal hysterectomy. There are, however, certain local complications to vaginal hysterectomy which merit consideration. They are not considered to be serious deterrents to the operation but are rather regarded as unavoidable postoperative nuisances.

The present report comprises a review of all vaginal vault complications which developed within the first year of postoperative follow-up in 96 patients subjected to vaginal hysterectomy. There is a single exception to the time of appearance of the several complications, inasmuch as one singular sequel appeared two years following vaginal hysterectomy. In each instance, the condition was sufficiently disturbing to warrant treatment.

Indications

Each type of hysterectomy, abdominal and vaginal, not being in any sense competitive, has its own indications and contraindications. The personal preference of the gynecologist often serves to heighten certain indications in respect to the type of operation.

The reasons for electing to perform vaginal hysterectomy in the 96 patients of this series are listed in Table I. The majority fall into the group of uterine prolapse. Some gynecologists do not consider prolapse of the uterus in women past the age of 40 to be an indication for vaginal hysterectomy; other gynecologic surgeons believe that it is. Siding with the latter group, I look upon vaginal hysterectomy as a safe and sound procedure in women beyond 40. The preservation by means of a more conservative procedure of a symptom-producing organ which has completed its reproductive function is something less than logical. It must, nevertheless, be emphasized that the Manchester type of operation is often applicable in younger women. The second group of patients subjected to vaginal hysterectomy includes women with abnormal uterine bleeding of benign origin for whom radical therapy is indicated. It is the conviction of many gynecologists that the uterus should be removed in every woman past the reproductive years who has, despite previous uterine curettage, continued uterine bleeding of abnormal character. The same comment may be made concerning the third indication for vaginal hysterectomy in this group, that of myoma. The remaining indications, in-

*Presented at a meeting of the Obstetrical Society of Philadelphia, Jan. 7, 1954.

cluding recurring polyps, dysmenorrhea, and carcinoma in situ of the cervix, require no explanation. The patient with carcinoma in situ did not require additional treatment inasmuch as histologic examination of the removed cervix showed no signs of invasion.

TABLE I. INDICATIONS FOR VAGINAL HYSTERECTOMY IN 96 WOMEN

INDICATION	NO. OF PATIENTS
Prolapse of uterus	40
Abnormal uterine bleeding	27
Leiomyoma of uterus	25
Recurring endocervical polyps	2
Dysmenorrhea	1
Carcinoma in situ	1
Total	96

Contraindications

There is a recognizable trend to broaden the indications for vaginal hysterectomy, undeniably salutary. I continue, however, to observe certain relatively fixed contraindications to the vaginal approach, as follows:

1. Fixation of pelvic structures as indicated by inability of the cervix to be drawn downward.
2. Malignant lesions of the genital organs.
3. Prior pelvic operations, such as uterine suspension, salpingectomy, cesarean section, and conservative surgery for endometriosis.
4. History of previous pelvic inflammation of a degree to render palpable abnormalities of the adnexa or cul-de-sac.
5. Massive uterine leiomyomas.

It is obvious from the wide scope of contraindications that the majority of patients encountered who require hysterectomy will be treated by means of the abdominal approach.

Present Report

This report is an analysis of 96 vaginal hysterectomies performed by me during the eighteen-year period, 1935 to 1952, a series composed only of private patients. The decision to exclude ward or service patients from this survey was based upon the fact that personal follow-up was not accomplished in them. I examined each of the 96 patients herein reported repeatedly during the first year after operation, the time when the vaginal vault complications constituting the body of this report, with a single exception, were observed in 39 of the group (40.6 per cent).

The local changes analyzed herein are sequelae to vaginal hysterectomy, which were either noted by the patient because of symptoms or observed by the examining physican. They followed both types of hysterectomy performed in this series, namely, Heaney and Mayo-modifications. It is not possible to estimate the ratio of vaginal sequelae to each of these techniques because this series is heavily weighted with Mayo-modification operations. Since prolapse of the uterus was the leading indication for performing vaginal hysterectomy and since I prefer to bridge stretched broad ligaments, more operations of Mayo type are included.

The sequelae encountered, shown in summary in Table II, are really troubles of the vaginal vault and include granulation tissue, enterocele, prolapse of the Fallopian tube, and endometriosis. Herniation of intestine through the vaginal vault, rather unique but noted in 1900 by Cullen,[1] and recurrent carcinoma were not observed. Absence of the latter is not surprising inasmuch as the sole patient of this series with carcinoma had only in situ growth.

Granulation Tissue

The incidence of granulation tissue in the vault of the vagina is less following vaginal hysterectomy than it is following abdominal hysterectomy but the degree of granulation is more. The vaginal granulations which follow abdominal hysterectomy appear as friable, soft, rather velvety polyps and do not occur in massive collections.

TABLE II. VAGINAL VAULT SEQUELAE FOLLOWING VAGINAL HYSTERECTOMY IN 96 WOMEN

SEQUEL	NO. OF PATIENTS	PER CENT
Granulations	31	32.3
Enterocele	4	4.1
Prolapse of oviduct	3	3.1
Endometriosis	1	1.1
Total	39	40.6

Granulation tissue, sufficient to disturb the patient or large enough to warrant therapy, was encountered in 31 of the 96 women (32.3 per cent). Of the 31 instances, 20 gave rise to leukorrhea or metrorrhagia and 11 did not. The gross appearance of granulation tissue of the vaginal vault varied in both quantity and quality, including velvety tags, red nodules, shallow ulcers, or pedunculated masses. On two occasions, the pedunculated granulation tissue was so large as to be suspected of being a prolapsed Fallopian tube. In fact, each patient was hospitalized for removal of a vault mass under the impression that it was an edematous oviduct. In one instance, the correct diagnosis was made during excision of the tissue; in the other instance, the proper diagnosis did not become apparent until the histological report was received from the pathologist.

The management of granulation tissue of the vaginal vault presents no especial problem. Twenty-nine of the 31 cases reported herein were eradicated by means of a fine-tipped electric cautery, the use of which was followed by the nightly intravaginal application of Triple Sulfa Cream for several weeks. The remaining two patients were those who presented massive tissue in the vaginal vault, which was suspected of being a prolapsed Fallopian tube and which was excised, as mentioned in the preceding paragraph. None of the 31 patients failed to heal properly.

Enterocele

Most gynecologists, admitting the possibility that overlooked enterocele may become prominent after vaginal hysterectomy, try to avoid it by means of sutures which approximate the sacrouterine ligaments and obliterate the

cul-de-sac. The refreshing, perhaps unique, experience of Thatcher and associates[2] is noteworthy, for they encountered no enterocele in follow-up of a large group subjected to vaginal hysterectomy.

Four instances of enterocele were encountered in the 96 patients herein reported (4.1 per cent). Three followed Mayo-type technique and one was a sequel to Heaney hysterectomy. Each of them was sufficiently disturbing to be noted by the patient within six months of operation.

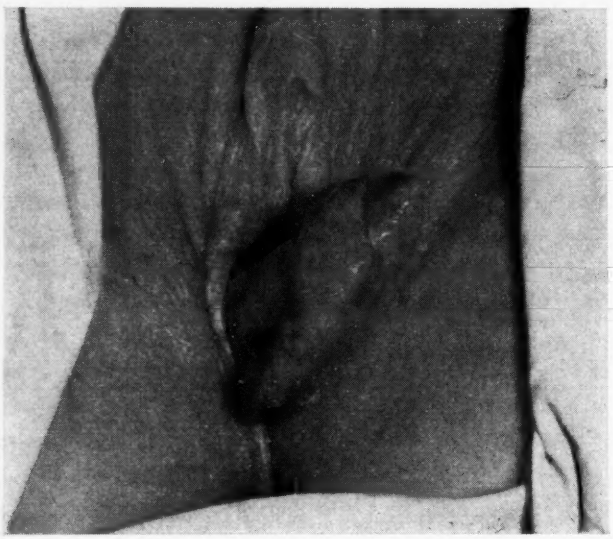

Fig. 1.—Prolapse of Fallopian tube two years after vaginal hysterectomy.

Treatment of the complicating enterocele varied somewhat. The primary indication for vaginal hysterectomy in the three patients who developed enterocele after the Mayo-type operation had been second-degree descent of the uterus accompanied by vaginal relaxation. Careful search for enterocele, real or potential, was made during the course of the initial operation. One of the three was recognized then and was allegedly repaired, only to recur within eight weeks of operation. It was of sufficient degree to bulge at the introitus. This was repaired vaginally but failed to heal properly. It was then successfully eliminated through the abdominal route by means of concentric obliteration of the cul-de-sac (Moschcowitz operation). The remaining two of the three which followed Mayo-type hysterectomy were not identified during operation but each made itself known within four months. Both were successfully repaired vaginally, by means of a technique which included isolation and elimination of the peritoneal sac, as well as approximation of tissue considered to be sacrouterine ligaments.

The single instance of complicating enterocele which followed a Heaney hysterectomy was, perhaps, the largest of the four and was unusual in that the bladder was one of the contents of the hernial sac. In fact, the bladder had so enlarged that it protruded, as part of the enterocele, from the vagina.

This patient was successfully treated by means of the Fletcher[3] operation of crossed support, a time-consuming abdominal approach which is apparently effective in selected instances.

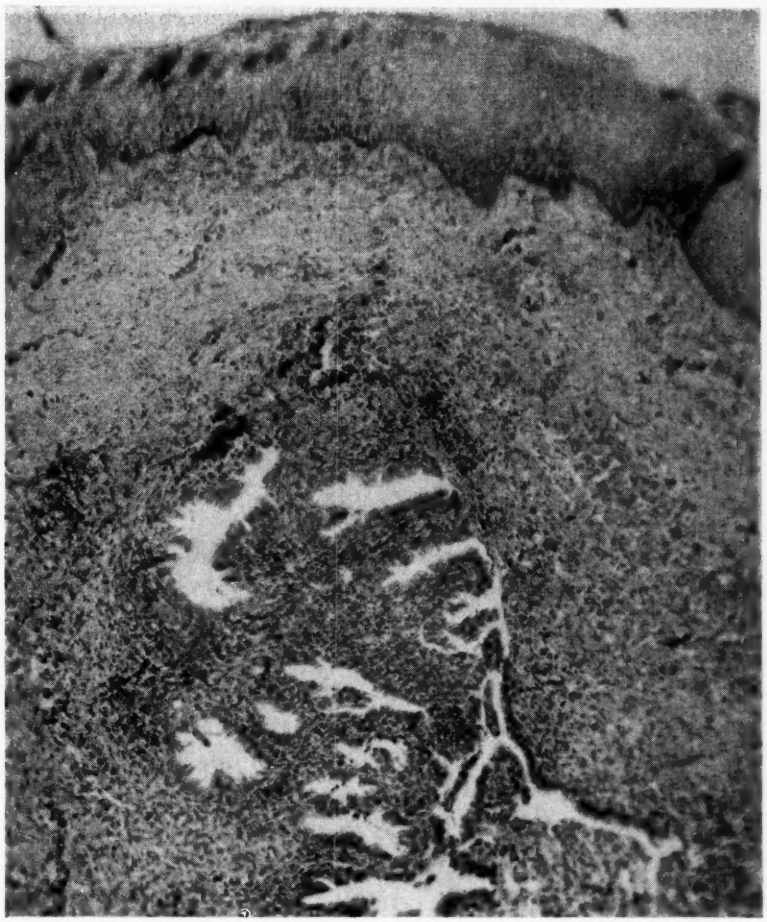

Fig. 2.—Endometriosis of vaginal vault following vaginal hysterectomy and oophorectomy because of endometrioma. (×80.)

Prolapsed Tube

The most dramatic of the local sequelae to vaginal hysterectomy is herniation of an oviduct through the vaginal vault. Three such complications were met in this series (3.1 per cent), two of which have been previously reported.[4] The third instance occurred in a 60-year-old woman who had been subjected to a Mayo-type vaginal hysterectomy because of second-degree descent of the uterus in October, 1951. Recovering from this operation without difficulty, she was observed to be well and to have attained an anatomically good result during an office examination in January, 1953. Six months later, in June, 1953, while stooping to pick up her grandchild, the patient was suddenly conscious of a protuberance from the vagina. Upon examination,

the mass was determined to be a Fallopian tube which lay outside the vagina for a length of three and three-fourths inches (Fig. 1). Treatment of this complication was simple in that the tube was excised as high as a ligature could be placed, following which the stump was observed to retract out of view, making closure of the small vaginal opening an easy task.

It is interesting to note that all previous reports of vaginal prolapse of the Fallopian tube following vaginal hysterectomy allude to the fact that this complication has not been observed following abdominal hysterectomy. In Heaney's[5] large series of vaginal hysterectomies, he mentions that he encountered "several instances of tubal prolapse" but does not describe them. Bonney,[6] noting tubal prolapse as "a possible complication" to vaginal hysterectomy, likewise details none. There have been less than 20 pathologically proved instances of such oviducal herniation reported.[4] It is important to recall that tissue removed from the vaginal vault as being that of Fallopian tube must be studied histologically in order to be certain of its identity. This is re-emphasized because of two experiences cited in the foregoing paragraphs to the effect that pedunculated granulations may mimic herniated Fallopian tube.

Endometriosis

One instance of vaginal endometriosis was encountered among the 96 patient (1.1 per cent). This occurred in a 38-year-old woman who had been subjected to a Heaney-type vaginal hysterectomy because of menorrhagia and leiomyomas of the uterus. During the course of hysterectomy, an endometrioma of the right ovary was discovered and right salpingo-oophorectomy performed. The pathologist confirmed the diagnosis of endometrioma. Four months following operation, a friable, bluish nodule approximately 1 cm. in diameter was noted in the center of the vaginal vault scar and was biopsied. It proved to be endometriosis (Fig. 2). The patient, observed closely during the next two years, reported the cyclic occurrence of slight vaginal bleeding at approximately monthly intervals. During this time, however, the endometriotic nodule doubled its size, finally being more than 3 cm. in diameter. At this point, postcoital bleeding was evoked on several occasions, creating sufficient anxiety to warrant treatment. Roentgen-ray castration was carried out and the patient apparently cured of metrorrhagia. The nodule lost its violaceous color and shrank to scarlike proportions.

Summary and Conclusions

This report has reviewed local sequelae encountered in 39 of 96 patients subjected to vaginal hysterectomy (40.6 per cent), including granulation tissue, enterocele, prolapsed Fallopian tube, and endometriosis. Each of these vaginal complications is sufficiently annoying to warrant therapy.

It is noted that enterocele may recur despite conscious effort by the surgeon to eliminate its presence at the time of vaginal hysterectomy. Abdominal operation to obliterate the cul-de-sac may be required in order to cure such recurrent herniation.

Granulation tissue, described as the most frequent vault complication following vaginal hysterectomy, may be so massive as to mimic prolapsed Fallopian tube. Two such examples are cited from the series reported.

None of the delayed complications described is an indictment of vaginal hysterectomy. This analysis merely re-emphasizes the need for careful post-operative follow-up.

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A TEN-YEAR STUDY OF TREATMENT AND ITS RESULTS IN INTRACTABLE PRURITUS VULVAE

A Supplementary Report of 228 Cases

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THIS is a supplementary report concerning 228 additional cases of intractable pruritus vulvae, from the Cook County Hospital Gynecologic Clinic and private practice. These were managed and followed from January, 1943, to January, 1953. The original report of 15 cases was made in June, 1943. This group was selected from a larger number of cases because each of these cases was followed for at least twelve months or longer. Therefore, absence of pruritus for twelve months or longer after the last injection was considered a "cure."

These patients complained of severe itching of the vulva. Close study by Papanicolaou smears, biopsies, and cultures eliminated such specific causes as Trichomonas vaginitis, Monilia, kraurosis and leukoplakia, ulcerations, dermatologic diseases, and systemic and metabolic conditions. Psychogenic etiology probably is an important consideration in some cases, and some of our series were referred from the psychiatric clinic. Because of lack of demonstrable etiology, we speak of intractable pruritus vulvae.

The gross appearance of the affected vulva varies in different patients. In some it presents no demonstrable gross abnormalities, while in others there are slight to moderate excoriations of the skin and some degree of redness. The more severe types show marked dermatitis, folliculitis, and fissures (¼ to 1 inch long) of the involved area. Not infrequently in the latter cases there is an accompanying pruritus ani.

The duration of the symptoms varied from six months to twenty-two years, the average being five years. The ages of the patients ranged from 28 to 72 years, the average being 45 years.

Since the last report, our technique has been modified. We have learned more about the effects of the medicament, and also about the time interval between the injection and the relief or cure of symptoms. The over-all results have been uniformly good.

We do not shave the pubic hair and we now use liquid detergent (1 part to 3 parts of warm water) or just soap and water to wash the vulva. Procaine (1 per cent) "wheals" are made with a 27 gauge hypodermic needle at the site of the entrance of the spinal needle. Through these wheals more procaine (about 2 to 3 c.c.) is injected with a hypodermic needle into the subcutaneous parts of the labia on both sides. These preliminary injections minimize or completely eliminate the pain when the large spinal needle is used to inject

the oil mixture (Fig. 1). Zylcaine* was used in our cases, but similar preparations may be employed. We have noted that the labia will vary in consistency and size, some being of average size, others smaller, but many are large and, therefore, will require more "oil." We now use from 5 to 10 c.c. for each labium and increase the amount from 2.5 to 5 c.c. for the supraclitoric and rectovaginal areas. One must always be mindful, however, of the all-important prophylactic consideration, that is, never to use enough "oil" to cause the overlying skin to become tense and thus lead to a slough. In this series we have not encountered a single slough.

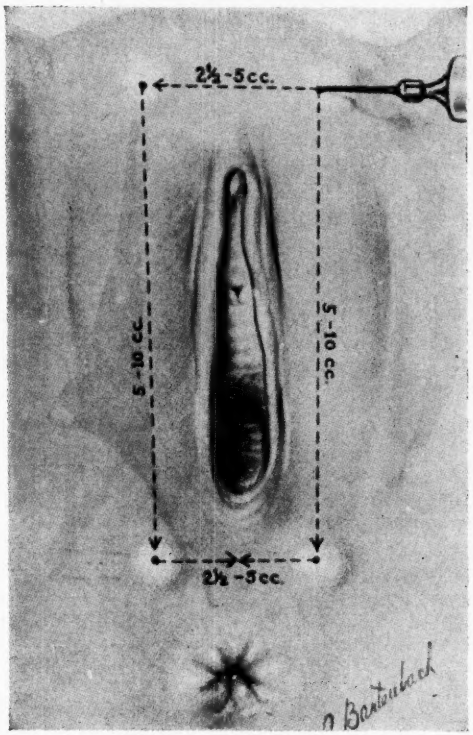

Fig. 1.—The technique of injection. Make four procaine wheals as shown, using a hypodermic needle and syringe. Follow the injection of procaine along the labia. This will make the "oil" injection painless. Fill a 20 c.c. syringe with slightly warmed Zylcaine. Use a 19 or 20 gauge spinal needle. Begin at the top and thrust the needle along the labia until you reach the lower pole. Inject the Zylcaine as you withdraw the syringe. Inject well beneath the skin to avoid a slough.

In our original publication, we reported that some of the patients were relieved within five to seven days. In this series, however, we encountered delayed "cures" or "reliefs." Some of the patients (see Tables) were relieved within a week, others in two weeks, while six required four to six weeks, one six to eight weeks, and some two and one-half months. We do not know the reason for this variation but shall attempt to explain this phase later in the text. There were two cases of allergic dermatitis in this group and one in the original series. In consultation with an allergist, we were advised to inquire of the patient whether there was a possible history of allergy to peanuts, peas, and beans, which items fall into the category of the peanut family, inasmuch as peanut oil is the vehicle of the medicament; or to have the patient "swish" a

*Zylcaine consists of procaine 1.5 per cent, Butesin 6 per cent, benzyl alcohol 5 per cent and peanut oil.

TABLE I. SUMMARY

TOTAL CASES	FAILURES	RELIEF OR CURE	NUMBER OF INJECTIONS	RACES		AGES
				WHITE	NEGRO	
228	18, or 7.8%	210, or 92.2%	19, or 9%, required 2 injections 4, or 1.9%, required 3 injections 187, or 89.1%, required 1 injection (Interval of injections was 2½ months)	160	68	28 to 72 years Average age, 45 years

TABLE II. TIME INTERVAL BETWEEN INJECTION AND RELIEF OR CURE OF ITCHING

Number of injections: 1

187, or 89.1%, were relieved in one week and were symptom free in from 2 to 4 weeks and remained without symptoms for 12 months or longer.

Number of injections: 2

19, or 9%

First week improved—about 25%
Second week improved—about 50%
Sixth week—there was recurrence of itching

Second injection: 12 weeks after the first injection
13th week—50% improvement
16 weeks after first injection or 4 weeks after the second injection—patient became symptom free and has remained so for 12 months or longer.

TABLE III. FOUR CASES, OR 1.9 PER CENT, WHICH REQUIRED THREE INJECTIONS

First week after first injection—improvement about 25%
Second week after first injection—about the same
Third week after first injection—about the same

Twelfth week: second injection
Thirteenth week after first injection—some improvement
Fourteenth week after first injection—improvement about 50%
Fifteenth week after injection—recurrence of itching
Sixteenth week after injection—recurrence of itching

Twenty-fourth week: third injection—75% improvement
Twenty-fifth week after injection—no itching at all and remained symptom free for 12 months or longer

The other 18 cases failed completely to respond to this treatment despite three injections.

TABLE IV. PATIENTS WHO FAILED TO RESPOND TO TREATMENT

6 who previously had x-ray treatments
1 patient with a psychoneurosis who was a chronic masturbator
11 patients with marked anxiety neurosis

All of them were given three injections but they failed to respond.

drop or two on her tongue, in order to detect any sensitivity. The most recent suggestion offered to us, which we have adopted, is the "patch test" for allergy. A drop of the oil is placed on the upper arm and covered with a plain Band-Aid; it is examined in twenty-four hours for any redness. If there is a reaction, we then test one of the many other anesthetic oils with different component parts. Eighteen of our patients failed to respond to this treatment.

Fig. 2.

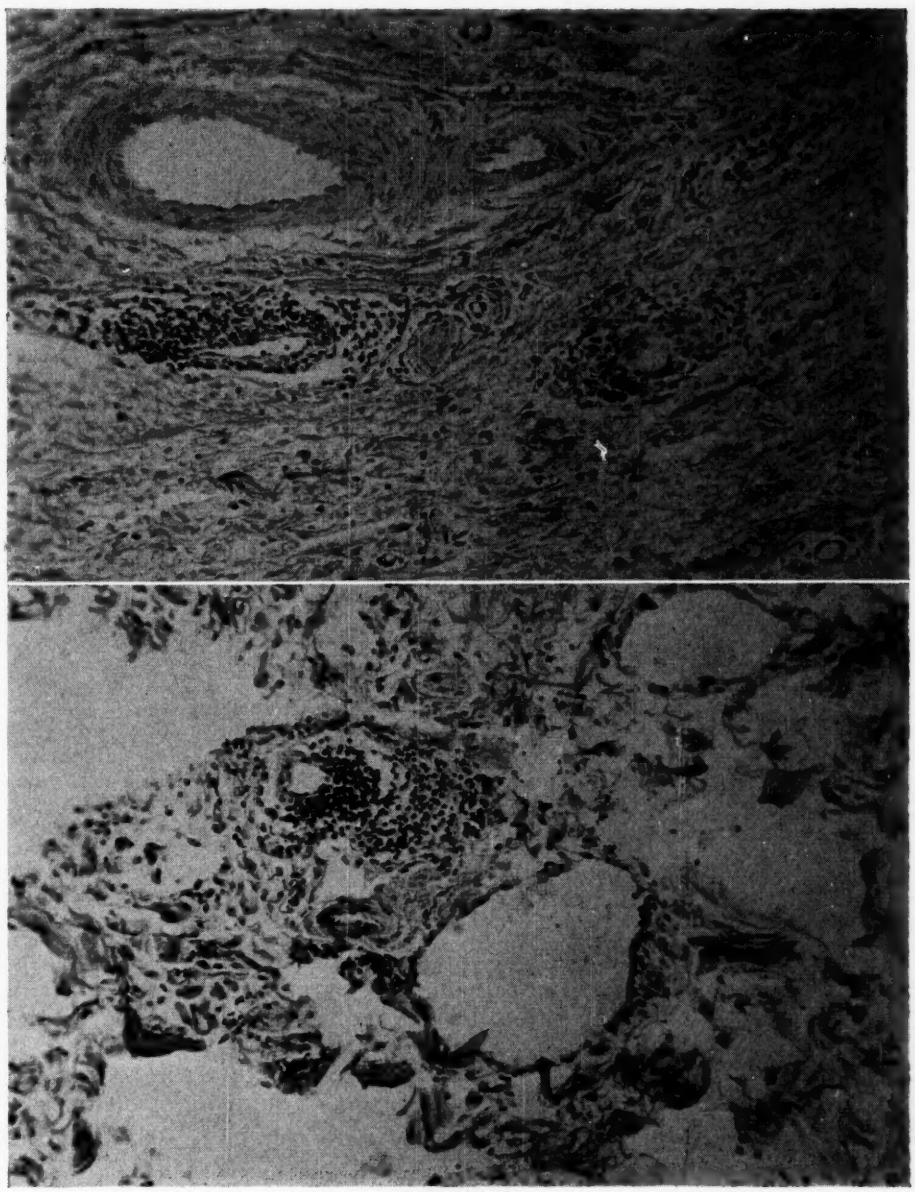

Fig. 3.

Fig. 2.—Microscopic examination reveals an intact epidermis and the subcutaneous tissues contain hair follicles and sweat glands. In the deeper layers of the subcutis, one sees accumulations of round cells and histiocytes about the vascular adventitia. (One week after injection.)

Fig. 3.—In the deeper layers of the subcutis, the perivascular accumulations of lymphocytes and plasma cells are readily seen. (Two weeks after injection.)

Six had previously received x-ray treatments and their skin was found to be sclerotic and lichenified. One patient was a neurotic and a habitual masturbator. The remainder were highly neurotic individuals.

Clinically the treatment is effective in a large percentage of cases. The modus operandi remained unknown to us. Investigation was undertaken in order to learn and to evaluate the probable action of the medicament. At first the abdominal wall of a dog was used, but it and the labia of the dog proved to be too thin for proper injection of the preparation; therefore, the human vulva was finally selected. A large wedge biopsy was made at weekly intervals for five weeks. The original biopsy of the labia before injection revealed nothing specific or pathogenic to identify it with the intractable pruritus.

Fig. 4.—The perivascular inflammatory reaction in the subcutis is much more prominent than in the previous sections, and *many of the smaller nerve trunks are firmly embedded in collagenous connective tissue.* (Three weeks after injection.)

Figs. 2 to 6 are photomicrographs of the biopsied tissue, stained with special nerve stains, and show the changes over a period of weeks. These may be summarized as follows:

Hematoxylin and eosin and van Gieson preparations indicate a nonspecific inflammatory reaction in the deeper layers of the subcutaneous tissue. In the succeeding weeks a progressive fibrosis is noted. We were unable to identify the oil in these sections and it seems likely that the oily substance diffused between the subcutis and the superficial fascia and, therefore, could not be found in the skin. The superficial nerves in the subcutis were compressed and this may have played a role in interrupting the pain cycle leading to the itching.

Comment

Pruritus may be considered a form of "pain," in that annoying stimuli bombard the brain producing conscious perceptions. Injection of the medicament and the subsequent reaction may alter the pain threshold without pro-

ducing any anesthesia of the vulva. The nerves in the subcutaneous tissues are compressed but not degenerated. It may raise the threshold of receptor organs and sensory nerve fibers, thereby stopping or reducing the itching. It is possible that this problem is similar to that found in ankle sprains in which the injection of Novocain results in much longer relief or cure than is the usual duration of anesthesia from Novocain itself. It is quite probable that

Fig. 5.

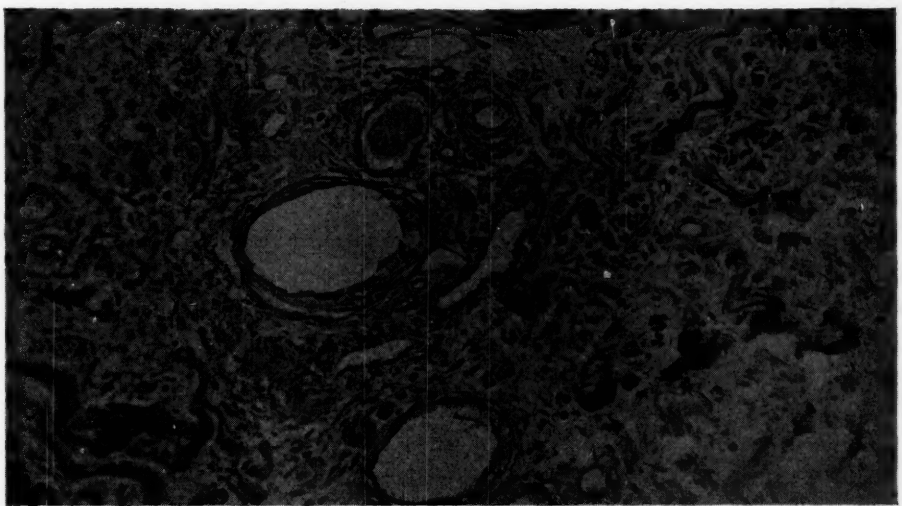

Fig. 6.

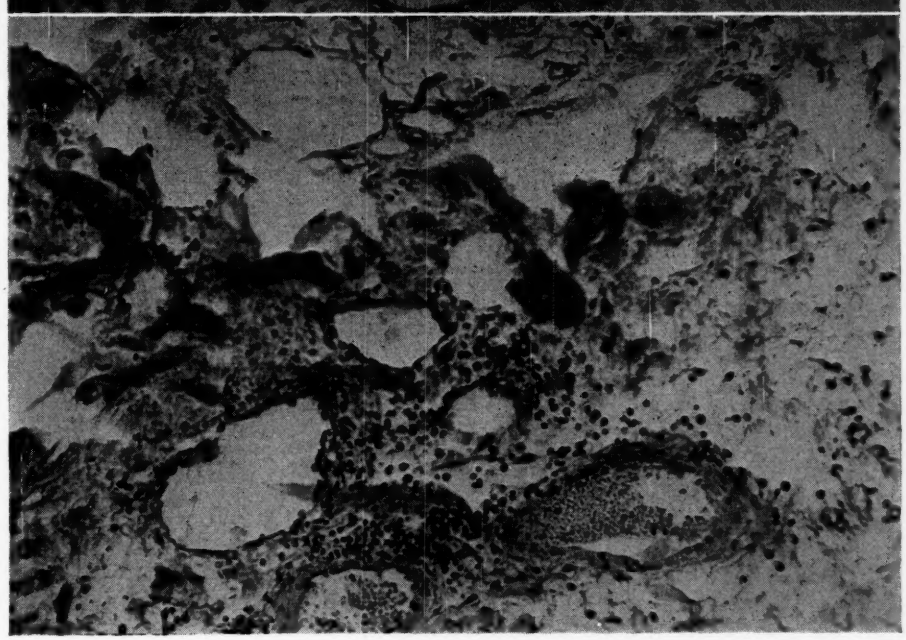

Fig. 5.—The subcutaneous fibrosis is much more intense and the inflammatory reaction has, for the most part, subsided. (Four weeks after injection.)

Fig. 6.—The subcutaneous fibrosis is quite marked but the perivascular inflammatory reaction is prominent with some evidence of organization, since fine reticular and collagenous fibers envelop clumps of inflammatory cells. (Five weeks after injection.)

the breaking of the pain cycle is the basis for the clinical results in these cases; also, that the reaction to the foreign body (medicament oil) by the deposits of fine connective tissue with a resultant compression of the nerve elements may account for the prolonged relief or cessation of symptoms. Novocain alone produces anesthesia of short duration.

Summary and Conclusions

A clinical report of a ten-year study of intractable pruritus vulvae is presented.

The time interval between the injection and the relief or cure of pruritus varies from one to eight weeks.

The histoneuropathogenesis following injection of the medicament in human beings is presented.

The probable modus operandi of the medicament and its relation to pain or pruritus are discussed.

The technique described is simple, practical, and safe. It needs no intricate apparatus or any special setup or assistance. It is done in the office, outpatient room in a hospital, or a clinic. Occasionally, however, if the patient is apprehensive, she may be given some form of intravenous anesthesia, such as Pentothal Sodium, and may either be kept in the hospital for twenty-four hours or be sent home the same day.

The texture and consistency of the labia return to normal within four weeks.

There is no permanent anesthesia of the skin overlying the vulva.

We wish to thank Dr. Ben Lichtenstein for the microscopic neuropathologic report and for his help in the preparation of this part of the paper.

THE VALUE OF CENTESIS AS A DIAGNOSTIC PROCEDURE IN RUPTURED ECTOPIC GESTATION

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THE increasing frequency of extrauterine gestation has been noted by many investigators, and has been thought to be one of the end results of antibiotic therapy in the treatment of acute and chronic salpingitis.[1, 2, 3] It has been postulated that the Fallopian tubes, although irreversibly damaged by infection, retain partial patency. Either because of pathological motility, narrowing of the lumen, or the formation of a pseudofollicular salpingitis, however, the zygote cannot reach the uterine cavity, resulting in the formation of a growing extrauterine pregnancy.

Both the prior existence of tubal infection and the relative and absolute increase in ectopic pregnancy have been noted. In reviewing our case histories, we found that in 82.7 per cent (312 of 378 cases) of proved ectopic gestations studied during the years 1947 to 1952, inclusive, there was either a history of antibiotic therapy for salpingitis, or a history of previous pelvic inflammatory disease. Furthermore, the number of extrauterine pregnancies has increased from year to year (Table I). That this is a true increase is noted, when the number of cases is compared with the number of gynecological admissions. A parallel increase also is noted when compared with the number of obstetrical deliveries at the same hospital.

Table I. Annual Numerical Study of Ectopic Pregnancy

YEAR	NUMBER GYNECOLOGICAL ADMISSIONS	NUMBER OF ECTOPIC PREGNANCIES	PER CENT OF ECTOPIC PREGNANCIES
1942	1,546	26	1.68
1943	1,746	31	1.77
1944	1,815	32	1.77
1945	2,199	30	1.36
1946	2,152	45	2.10
1947	2,079	44	2.12
1948	2,160	49	2.22
1949	1,961	59	3.01
1950	1,906	88	4.64
1951	2,096	71	3.38
1952	2,211	62	2.82

It is almost universally agreed that tubal gestation presents only the signs and symptoms of early intrauterine pregnancy, and cannot easily be diagnosed until that time in its development when rupture of the tube, erosion of a blood vessel, or extrusion of the fetus from the fimbriated end of the tube occurs. Symptoms and findings develop rapidly, and range from minimal to catas-

trophic in nature. These may mimic any disease of the lower abdomen, occasionally disease of the upper abdomen, and, rarely, even disorders of the chest. Davidson and Mandelbaum[4] have expressed dissatisfaction with the high percentage of diagnostic errors, and have attempted, with only partial success, to find a pattern of history and diagnostic procedures which would aid in improving the early diagnosis of this disorder.

Since intra-abdominal bleeding must accompany either rupture or erosion of the tube, considerable stress has been placed on needle aspiration of the pouch of Douglas, with the thought that the recovery of sanguineous fluid would be of greatest value in either making or confirming the diagnosis of a ruptured tubal gestation. Kole[5] reported 95 per cent correct results from such aspiration of the posterior cul-de-sac. Word[6] found cul-de-sac punctures positive in 51 of 53 patients, false negatives being reported in 2, and false positive results in 3 others. It is the purpose of this paper to evaluate, on the basis of our experiences, the merits of centesis for the diagnosis of ruptured ectopic pregnancy and tubal abortion. We do not propose to include in such an evaluation any of the many other criteria of history or physical findings which may be utilized for reaching such a diagnosis.

For this study, we have reviewed cases where ectopic pregnancy was the preoperative diagnosis, or where such a diagnosis was made on exploratory laparotomy. Cases of suspected ectopic pregnancy which were later diagnosed as being other gynecological or surgical disorders are neither considered nor included. The group studied covers a period of five years and includes a total number of 431 operative procedures. Preoperative diagnoses and postoperative findings are given in Table II.

TABLE II. FIVE-YEAR STUDY OF LAPAROTOMIES FOR ECTOPIC PREGNANCY
431 CASES

TOTAL OPERATIONS FOR ECTOPIC PREGNANCIES	NUMBER OF ECTOPIC PREGNANCIES	DIAGNOSIS MADE AND FOUND	DIAGNOSIS MADE AND NOT FOUND	DIAGNOSIS NOT MADE AND FOUND
431	373	352	58	21
100%	86.5%	81.6%	13.3%	4.9%

From Table II it can be readily seen that a correct preoperative diagnosis of ruptured ectopic pregnancy or tubal abortion was made in only four out of five cases operated upon. Actually, less than 82 per cent of all such cases seen were correctly diagnosed before surgery was instituted. What is of greater significance is the fact that 58 women (13.3 per cent) underwent unnecessary emergency surgery because of an incorrect preoperative diagnosis.

Since intra-abdominal bleeding accompanies tubal rupture, and since such hemoperitoneum should be picked up by tapping, we have attempted to coordinate the use of centesis with the findings on laparotomy. Hemoperitoneum following the rupture of a tubal pregnancy, an interstitial pregnancy, or a tubal abortion may be demonstrated by culdoscopy, aspiration of the cul-de-sac, and paracentesis. Culdoscopy, as proposed by Decker,[7] although often employed in a differential diagnosis, especially of an unruptured tubal pregnancy, can offer little additional information in acute cases. This procedure requires anesthesia and the knee-chest position. It is time consuming at a period when time is often at a premium. As will be shown later, however, it may have definite value in certain controversial and equivocal cases. On the

other hand, objections to cul-de-sac aspiration and paracentesis have been raised on the basis of the possibility of introduction of infection, of possible misinterpretation of either positive or negative findings, and of the uncertainty of correct technique.

These procedures, however, have certain value, in that the techniques are simple and quick, and they can be done in the routine course of examination without anesthesia. To perform a cul-de-sac puncture a sterile speculum is inserted into the vagina, and the posterior lip of the cervix grasped with a tenaculum and elevated. A 4 inch, 18 or larger gauge needle, attached to a syringe, is inserted sharply into the posterior fornix and is pushed inward, along an axis parallel to the posterior wall of the uterus for a distance of 2 to 5 cm. Minimal suction is then applied. Paracentesis likewise is simple, easy, and quick. After an area approximately 3 cm. medial to the iliac spine is cleansed and sterilized, a small amount of procaine is introduced under the skin, and a long needle, similar to the one for cul-de-sac aspiration, is inserted downward and medially in such a manner that the point approaches the area of the Fallopian tube. The suspected side is usually probed first, but both sides may be tested as deemed necessary.

Results

All results of centesis are interpreted on the basis of the presence and type of fluid withdrawn into the syringe. A tap is considered as negative when, after assurance that the lumen of the needle is in the peritoneal cavity, no fluid of any type is withdrawn. An equivocal tap, usually to be considered as negative, is diagnosed when blood which is bright red and which clots is aspirated. The presence of pus in the aspirated fluid is indicative of intraperitoneal infection. The presence of serum, plasma, or clear fluid in most cases must be considered as equivocally positive, as will be discussed later. The removal of blood which is not clotted, and which will not clot on standing, or which may contain small dark clots is to be considered a positive test for hemoperitoneum. In Table III are expressed the results obtained by cul-de-sac aspiration and paracentesis in the evaluation of the diagnosis of the presence of intraperitoneal bleeding occurring with the rupture of an ectopic gestation or a tubal abortion.

TABLE III. RESULTS OF CUL-DE-SAC ASPIRATION AND PARACENTESIS IN RUPTURED ECTOPIC GESTATION

	DIAGNOSIS ECTOPIC PREGNANCY MADE AND FOUND	DIAGNOSIS ECTOPIC PREGNANCY MADE AND NOT FOUND
Total number of cases (1947-1952)	352	58
Cul-de-sac aspiration performed	160	33
Positive punctures*	128 (80%)	3 (9%)
Negative punctures	32 (20%)	30 (91%)
Paracentesis after cul-de-sac aspiration*	16	6
Positive paracentesis	9	0
Total positive centesis	137 (85%)	

*These statistics include 7 cases where clear serous or blood-tinged serous fluid was obtained on cul-de-sac aspiration.

From Table III it can be readily noted that in 160 cases of ectopic pregnancy where cul-de-sac aspiration was used as a diagnostic criterion for hemoperitoneum, 80 per cent of the cul-de-sac punctures performed gave correct positive reports. When 9 positive paracenteses are added, the correct percentage of diagnoses was 85 per cent. Of the 58 misdiagnosed cases 30, or 91 per cent, negative cul-de-sac taps were correctly negative. Therefore it

appears at first glance that these procedures have a definite value as a method for diagnosis. It can also be readily noted from this table, however, that both positive and negative errors were obtained when results of abdominal taps were compared with results on laparotomy.

Moreover, the value of the intra-abdominal aspiration must be considered, not only in the light of correct percentages of results, but also as a true diagnostic aid where other procedures are doubtful, incomplete, or misleading. In a critical analysis of the data presented in Table III, 57 per cent (192 of 352) of the cases of proved ruptured ectopic gestation or tubal abortion were correctly diagnosed without the use of either cul-de-sac aspiration or paracentesis. Also, in this critical study of all case histories, it was felt that in 75 per cent of the 160 cases where these procedures were employed, centesis was merely of adjunctive value, the correct diagnosis having been reached independently by means of history and physical findings alone. Thus, in all but 40 cases (25 per cent) a correct diagnosis was made without the actual need for needle aspiration. It is in these 40 cases, however, because of equivocality of physical findings and history, that intra-abdominal centesis, if of any value, should give reliable results. In this group of 40 cases, differential diagnoses ranged from postabortal peritonitis to twisted ovarian cysts, and included ruptured appendix, acute appendicitis, leaking tuboovarian abscesses, and incomplete abortion. Therefore, a separate, critical, and complete review of these 40 cases was made, using the criteria of cul-de-sac and abdominal centesis as the main diagnostic measure for determining the presence of a ruptured tubal gestation or a tubal abortion. This study is expressed schematically in Table IV.

TABLE IV. VALUE OF CENTESIS IN EQUIVOCAL DIAGNOSES OF RUPTURED ECTOPIC GESTATION, 40 CASES

Correct positive cul-de-sac aspiration		11 cases	(27.5%)
Hemoperitoneum	7 cases		
Serum	4 cases		
Correct negative cul-de-sac aspiration		11 cases	(27.5%)
Incorrect negative cul-de-sac aspiration		15 cases	(37.5%)
Incorrect positive cul-de-sac aspiration		3 cases	(9.0%)
Correct abdominal taps (after negative cul-de-sac aspiration)		4 cases	
Per cent correct cul-de-sac aspiration		55	
Per cent correct cul-de-sac aspiration and paracentesis		65	
Per cent erroneous taps		35	

Thus, although paracentesis and cul-de-sac aspiration are apparently valuable in the diagnosis of ruptured ectopic gestation and tubal abortion, it can be seen that their accuracy is markedly decreased when only equivocal cases are considered. In order better to understand the value of centesis, and to interpret and explain the data listed in the tables, it is necessary briefly to discuss the sequence of events which occur with the rupture of any extrauterine pregnancy.

Comment

In the evaluation of centesis as a diagnostic procedure for ruptured extrauterine gestation, all results must be classified into (1) correct positive taps, (2) correct negative taps, (3) incorrect positive taps, and (4) incorrect negative taps. Extrauterine pregnancy gives few or no symptoms until such a time as bleeding occurs from the rupture of the tube or abortion of the pregnancy through its fimbriated end. The physical status of the patient, the findings on

examination, and the results of aspiration of the cul-de-sac or the abdominal cavity proper are directly dependent upon the rapidity of bleeding, the amount of blood loss, and the amount of blood in the abdominal cavity.

1. Correct Positive Centesis.—These cases included all those where unclotted and unclottable blood was withdrawn, whether through the cul-de-sac or through the abdominal wall. Correct results were obtained in 80 per cent of those cases tested by cul-de-sac aspiration alone, and in 85 per cent of cases where combined cul-de-sac aspiration and paracentesis were performed. Intra-abdominal bleeding and clotting follow the same coagulation pattern as does the extravasation of blood elsewhere in the body. In the peritoneal cavity, however, the blood tends to become defibrinated, because of the whipping effect of the peristaltic action of the intestines. Therefore, with the loss of fibrin, the blood again becomes fluid, and can easily be aspirated by means of a centesis needle, thus giving a positive tap.

A small hematoma may develop about the embryo in the tube without blood loss into the abdominal cavity. With minimal bleeding, however, which may occur with tubal abortion, or with a small rupture of the tubal wall, clots may form and remain localized around the area of the tube. This is especially true when pelvic adhesions resulting from inflammatory disease are present. These adhesions may retard the dissemination of the clot or may form a nidus for its adherence and localization. When such a condition is present it is obvious that a tap through the cul-de-sac will be falsely negative. If with minimal bleeding, however, a paracentesis is performed in such a manner that the lumen of the needle is in the area of the localized extravasated blood, a productive tap confirming the diagnosis will be found. Such a sequence is illustrated by the following case:

No. 16571—Mrs. B. C., a 28-year-old Negro woman, para ii, gravida iv, was admitted to the hospital on October 1, with the history of lower abdominal pain of 2 weeks' duration, which pain was gradually increasing. The last menstrual period was August 9, apparently normal. There was a history of "tubal inflammation" four years previously. There had been no pregnancies since, and no history of dizziness or fainting.

Physical examination revealed an extremely well-nourished, obese woman in no apparent distress. The breasts were negative, with no secretion present. The heart and lungs were negative; the abdomen was slightly distended and rigid, tender in both lower quadrants, with some questionable rebound tenderness on the left side. Vaginal examination revealed normal external genitals, and a normal vagina. No external vaginal bleeding was present. The cervix was axial and slightly tender on motion. The fundus was apparently normal in size and consistency. A questionable cystic mass was palpated in the right adnexa.

The blood pressure was 144/84 mm. Hg; pulse 74 per minute; temperature 99.4° F.; hemoglobin 11.0 Gm.

Because the differential diagnosis included possible ectopic gestation, cul-de-sac puncture was performed on two occasions. Both taps were negative. At the time of the second negative puncture an abdominal tap was done on the right side which was positive for old blood and clots.

Laparotomy was performed on October 5. Findings on operation were minimal abdominal bleeding, intestinal adhesions to the top of the fundus, right broad ligament, and

both tubes. After separation of the adhesions, a tubal abortion was found on the right side, which was surrounded by many blood clots. A right salpingo-oophorectomy was performed. The patient's recovery was good.

The pathological report was tubal gestation, tubal abortion; chronic salpingitis; corpus luteum of pregnancy in ovary.

This case demonstrates the value of paracentesis when hemoperitoneum cannot be demonstrated by needle puncture of the posterior fornix. Abdominal paracentesis on either one or both sides is therefore the next diagnostic procedure of choice following a negative cul-de-sac aspiration in all suspected cases.

The localization and retention of the blood clot as described may lead to the recovery of serum or serumlike liquid on aspiration of the cul-de-sac. We have observed 9 such taps, and on laparotomy confirmed the presence of a ruptured ectopic pregnancy. The blood clots, held in a more or less fixed position around and in the ruptured tube, will, after the passage of time, begin to contract, causing extrusion of serum. This, being liquid, will gravitate into the posterior fornix and be recoverable on needle aspiration. This fluid when found on puncture must be differentiated from ascitic fluid produced either by a twisted ovarian cyst or by a pelvic tumor mass, by means of hematin assay. Illustrative of this type of case is the following:

No. 17261—M. B., a 27-year-old Negro woman, para 0, gravida i, was admitted on October 26, with the complaints of respiratory pain, upper abdominal distress, and vomiting of three weeks' duration. The patient fainted on admission. She was first seen on the medical service and transferred to the gynecological service. The last menstrual period had been approximately four months previously. She stained for two months at the time of her expected menses but there had been no bleeding or staining for the last eight weeks. The remainder of the history was without significance.

Physical examination revealed a well-nourished woman appearing slightly pale, but apparently not in pain or distress. The breasts were negative for secretion. The heart and lungs were within expected limits. The abdomen was soft and flat, with a tender spot in the suprapubic area and in the lower left quadrant. No rebound tenderness was elicited. On vaginal examination, the external genitals were normal. There was no vaginal bleeding. The cervix was slightly softened and slightly tender on motion. The uterus was anteverted, of normal size and consistency. An indefinite mass approximately 10 cm. in diameter was thought to be felt in the right adnexa.

The blood pressure was 110/70 mm. Hg; pulse 80 per minute; the erythrocyte sedimentation rate was within normal limits; hemoglobin 10.0 Gm.

Cul-de-sac puncture yielded clear yellow, slightly blood-tinged, serumlike fluid.

The patient was observed for twenty-eight hours, with a differential diagnosis of twisted ovarian cyst, possible appendicitis, leaking tuboovarian abscess or ectopic pregnancy, after which an exploratory laparotomy was performed. On examination of the abdominal viscera, many localized blood clots were found around the region of the fimbriated end of the right tube. There was no generalized hemoperitoneum. Below these clots a right tubal abortion was found.

A right salpingectomy was performed. Recovery was good.

The pathological report was tubal abortion, hematosalpinx.

Thus, from our observations, positive taps must be considered to include: (1) those in which unclotted and unclottable blood is withdrawn from the cul-de-sac, (2) those in which, even though a negative cul-de-sac aspiration is

noted, positive results are obtained with the removal of a similar sanguineous fluid through the abdominal wall, and (3) those in which serum is withdrawn from the cul-de-sac on puncture. In other words, when centesis is to be used as a diagnostic measure, all negative cul-de-sac punctures should be followed routinely by abdominal taps. With this double procedure a higher percentage of correct results was obtained. Using these criteria, correctly positive centeses were obtained in 85 per cent of the 160 cases studied. This corresponds favorably with the results of other investigators.

2. Correct Negative Taps.—Little is to be said for those cases where taps were found to be negative and no hemoperitoneum was noted on laparotomy. In the entire series, 91 per cent of the cases incorrectly diagnosed and operated upon were found to have correct negative cul-de-sac aspirations and paracentesis.

3. Incorrect Positive Taps.—In the present study, 3 cases were diagnosed as ruptured ectopic gestations on the basis of false positive cul-de-sac punctures. Of these, one patient gave an almost perfect history of a ruptured ectopic pregnancy, including a history of skipped menses, irregular spotting, and sudden onset of pain accompanied by an episode of fainting. On abdominal exploration the hemoperitoneum was found to be due to a rupture of the spleen. In the remaining two cases, cul-de-sac taps were positive, but on surgery, examination of the abdominal viscera was negative, the peritoneal cavity was free of blood, and the pelvic organs normal. Both these taps must be considered to be incorrect due to perforation of a pelvic blood vessel or uterine sinus. No explanation can be offered as to why the blood seemed to remain fluid in the syringe and not clot, even on standing for a considerable time.

4. False Negative Taps.—In the series studied 32 (20 per cent) of proved cases of ectopic gestation gave false negative cul-de-sac punctures. Several explanations may be offered for this. These include (1) the presence of localized blood clots as previously discussed; (2) faulty technique, the needle lumen remaining outside the peritoneum either in the wall of the uterus or in the layers of the endopelvic fascias below the peritoneum; (3) large clots filling the cul-de-sac which could not be aspirated because rapid and vigorous intraperitoneal bleeding had prevented blood defibrination.

Summary

Over a period of five years, a study was conducted to determine the value of cul-de-sac aspiration and paracentesis as a diagnostic aid in the differential diagnosis of pelvic conditions which conform to no rule or standard and when ectopic pregnancy or a tubal abortion was considered. This study includes a series of 431 laparotomies where such a provisional diagnosis of extrauterine pregnancy was made prior to surgery or where ectopic gestation was found as an incidental factor on operation. Of these, 373 actual extrauterine pregnancies were found. Diagnosis was made prior to surgery correctly in 81.6 per cent of the total number of cases operated upon; 13.3 per cent were incorrectly diagnosed and operated upon.

It was felt that because of the varied and variable pictures presented by such a condition, and because of the need of a rapid and essentially correct diagnostic procedure, aspiration of the cul-de-sac and paracentesis might be of value. Furthermore, it was felt that centeses were essentially without harm and could be employed without any special apparatus or technique. Results obtained were rapid, and would be of immediate assistance, in a situation where an actual gynecological emergency might exist. A total of 193 such punctures were made, 160 in cases later proved by surgery to be ruptured extrauterine pregnancies, and 33 where no such pathology was found.

It was found that cul-de-sac puncture alone was correct in 80 per cent of the cases tested. When paracentesis was used as an adjunctive procedure following negative cul-de-sac aspiration, the average of correct positive diagnoses was about 85 per cent. Likewise, in 58 cases where no ectopic gestation was found on operation, cul-de-sac aspiration gave 91 per cent correct results. Despite these apparently good averages, false positive punctures (9 per cent) and false negative results (20 per cent) were obtained. It was found, furthermore, that cul-de-sac aspiration, when negative, did not exclude the presence of a tubal abortion since in 9 cases a positive paracentesis was obtained after a negative cul-de-sac aspiration.

In 75 per cent of all cases, however, the correct diagnosis had been reached without the primary support of taps, and on the basis of the history and physical examination alone. In the remaining 25 per cent (40 cases) diagnosis was most difficult because of equivocal history and physical findings. It was felt that in this group the value of centesis might be demonstrated. In a critical study of these cases, however, it was found that cul-de-sac aspiration was correct in only 55 per cent of the cases studied. When followed by paracentesis, the correct average is 65 per cent.

Despite the fact that the procedure of centesis is not a totally accurate one, we have felt that, because of ease of performance and rapidity of results, it has a definite value for verification of the diagnosis of ruptured tubal gestation and tubal abortion. It is not, however, a procedure which can replace good clinical judgment and discernment, nor is it a procedure which has the ability to produce a correct result when the amount of bleeding into the peritoneal cavity is minimal or localized. This does not detract from its value, since emergency surgery is not imperative in those cases where the diagnosis is in doubt and other measures including watchful observation and culdoscopy can be performed. Centesis, both through the cul-de-sac and through the abdominal wall, when properly performed, is felt, on the basis of this study, to be a procedure which may be considered a help in diagnosis of suspected tubal abortion or ruptured tubal gestation.

Conclusions

1. The increasing number of ectopic gestations has been noted.

2. The value of centesis has been studied as a diagnostic measure for ruptured tubal gestation. Aspiration of the cul-de-sac gave accurate results in

80 per cent of the cases of proved ectopic pregnancy, and 91 per cent of the cases where no extrauterine pregnancy was present. Paracentesis following negative cul-de-sac punctures improved the average of correct positive results to 85 per cent.

3. Both false positive and false negative centeses were noted.

4. In those cases where minimal hemoperitoneum results from a ruptured tubal pregnancy or tubal abortion, both symptoms and centeses are equivocal. In such cases, paracentesis and aspiration of the cul-de-sac give no better than 65 per cent correct results.

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A TRIBUTE TO RUDOLPH WIESER HOLMES*

RALPH E. CAMPBELL, M.D., MADISON, WIS.

I AM appearing before you with conflicting emotions. I feel a deep honor in giving the initial presentation of the Rudolph Wieser Holmes and Maria Baxter Holmes Fund in memorial to their mothers, Paula Wieser Holmes and Sarah Moore Baxter, but I am very sorry that Dr. Holmes could not live for this meeting.

Dr. Rudolph Wieser Holmes was known to many of you as colleague, to some as teacher, but to all as a friend. He was born June 27, 1870, in Chicago. He graduated from the Harvard School and Harvard College, then graduated from Rush Medical College in 1893. He interned at Presbyterian Hospital in Chicago from 1894 to 1895. Following his marriage to Maria Baxter in 1898, he studied in Dresden, Vienna, Prague, and Berlin.

Attesting to his prominence in obstetrics, Dr. Holmes was Attending Obstetrician at the Chicago Lying-in Hospital and Dispensary, Cook County Hospital, Passavant Memorial, and Augustana Hospitals. He was also President of the Passavant Staff from 1908 to 1925. He was a consulting obstetrician at the Chicago Maternity Center from 1930 to 1940.

Dr. Holmes was a professor of obstetrics at Rush Medical School, becoming an emeritus professor in 1927 due to ill health. In 1929 he became Associate Professor of Obstetrics at Northwestern Medical School and Director of Obstetrics at Passavant Hospital, posts he held until 1936. He was recalled from retirement at Charlottesville, Virginia, by Dr. Irving S. Cutter, Dean of the Northwestern University Medical School, to organize a department of obstetrics at Passavant Hospital. I would like to read his letter of acceptance to Dr. Cutter which was dated June 1, 1929, and reads as follows:

"In accepting the medical school appointment, I had but one great desire, that I might do my utmost to make the obstetric department of the hospital worthy of the building which houses it and that I might again have a period of teaching. Have been slow in accepting the appointment in the medical school, but my hesitation was based on the fear that my physical condition might militate against an adequate devotion for the tasks set before me. But in accepting the place, I would have you know that my years of loyalty to the hospital will be reflected in as great a loyalty to the school."

Dr. Holmes was very active in medical groups throughout the United States and was President of the Chicago Gynecological Society, 1912-1913; President of the Central Association of Obstetricians and Gynecologists, which

*Presented at a meeting of the Chicago Gynecological Society, Nov. 20, 1953.

he had helped to found, 1930-1931. He was a director of the American Committee on Maternal Welfare and Treasurer of the American Congress on Obstetrics and Gynecology for many years. He was Chairman of the Committee on Graduate Teaching of the White House Conference. Dr. Holmes was among those very active in the formation of the Joint Committee of Maternal Welfare of Cook County in the early days. He was listed in *Who's Who in America.*

Among his many contributions to the literature were: chapters on "Puerperal Hemorrhages" and "Malposition of the Fetus" in Davis' textbook, *Obstetrics and Gynecology;* articles on "The Maternal Ward of a General Hospital," "A Survey of the Operative Incidence and Mortalities in Four Hundred Forty-Five Hospitals," "Ablatio Placentae," "Institutional Obstetrics," "Cesarian Section, a Phase in the Unwise Modern Obstetric Trend," and "Obstetrics and Gynecology, Their Unity in Practice and Pedagogy," Presidential Address before the Central Association.

There were many others, but this will show you what a varied interest he had, but always with one over-all theme, "Maternal Welfare."

Before his death, Dr. Holmes had hoped to be present at the introduction of the fund in the memory of his mother and Mrs. Holmes' mother and we had many letters in regard to the subject. I would like to read his initial letter dated Nov. 15, 1952, on this matter so that you can better understand what he had in mind. It reads as follows:

"I know not if you are aware that in 1947, after I lost Mrs. Holmes, I was settlor of a Trust, which, after my death, was to become effective for two purposes, primarily for the promulgation of matters pertaining to Maternal Welfare, as a memorial to our respective mothers, and secondly as a memorial to my father on matters especially pertaining to Ophthalmolgy.

"In our joint lives we had in our respective wills the provision that the Trust would be created through the will of the survivor. After her loss, I could not do else but to anticipate my own death, and complete the indenture in my life, rather than let some other person do it for me. Over four years ago, under the auspices of the Institute of Medicine, I arranged for a presentation as a first tribute to my father. Lately, certain matters arose and I began to dwell on the plan of having the introductory presentation of the Maternal Welfare division as the memorial to our mothers.

"I do not have an ironclad plan that either one or the other should be of material latitude—that first the incomes should be expended upon grants for investigation, awards to young men especially for original research, or original contributions to what was new.

"As my father's share of the memorial was under the direction of the Institute of Medicine, so the primary part, the Maternal Welfare, should be directed by the Chicago Community Trust (and I add with the Northern Trust of Chicago as Trustee) with a medical committee organized by an advi-

sory board, as I firmly believe that the choice of annual award should be selected by an obstetric board, as such a board will better appreciate the needs than will a layman.

"As my first paper on Obstetrics was presented before the Chicago Gynecological Society in 1901, as a matter of sentiment I have felt it appropriate that the introductory presentation on Maternal Welfare should be presented before the same society. Also, as a very personal desire, I would like to have this session in the May meeting of the above Society, which takes place on the third Friday of the month. In a tentative way I have asked Doctor DeCosta to reserve time that evening."

It was Dr. Holmes' intent to be present at a meeting scheduled for May 15, 1953, before the Chicago Gynecological Society; however, he died on April 25, 1953, and it was decided that the meeting should be postponed to a later date inasmuch as his death would change the character of the meeting.

Dr. Holmes wished for no eulogy for himself and I would like to read from one of his letters: "You have stated that May 15th has been set aside by The Chicago Gynecological Society in my honor. That thought were far from my desires: my one idea has been that I might live long enough to see the dream which Mrs. Holmes and I had had for many years come true: on that occasion I would wish to have a very incidental part—I necessarily, must appear in the picture that it would be complete; I would beg of you not to let there be any obtruding thought to mar the main issues that the occasion is a memorial to our Mothers and the beginning of a contribution to enhance benefits for all motherhood. Beyond that I would not desire to appear.

"If the turn of events should come upon me that would preclude my coming to the meeting I have asked the Chicago Community Trust, and so ask you that the plan we have made shall be consummated. I trust that such an exigency shall not arise, for all the years I was in residence in Chicago, the Third Friday of the month booked no interference."

In paying tribute to Dr. Holmes, it is necessary to tell something of the women who were so loved by him that he wished to honor them with this memorial fund.

Paula Wieser Holmes was born in Agram, Austria, in April of 1830. She married Edward Lorenzo Holmes in 1862 and they came to Chicago to make their home. Dr. Edward Holmes was a pioneer physician and surgeon and practiced in Chicago for many years. Upon her arrival in Chicago, Mrs. Holmes knew practically no English, but overcame this barrier quickly and was one of Chicago's most charming and talented hostesses. She was a gentle woman but a very inspiring one and Dr. Holmes often said that his mother was his original inspiration.

Sarah Moore Baxter was at all times delightful company. She was an excellent mother and trained her daughters to be resourceful and domestic. She had been remembered by her granddaughter as a small, charming old lady.

Dr. Holmes gave to many worth-while youth movements and wished in most cases to remain anonymous. He was particularly interested in the Young Peoples Group of St. Chrysostom's Church of Chicago and often gave them contributions.

Dr. and Mrs. Holmes established the Paula Wieser Holmes and Sarah Moore Baxter Memorial in the Rush Medical College Library.

When Dr. and Mrs. Holmes lived in Chicago, they had frequent open house for residents, interns, and students. Dr. Holmes helped many students when they were financially unable to continue their medical work without such aid.

Dr. Holmes was a living example of one of his father's remarks to a graduating class of Rush Memorial School: "May each of you grow old and wear out in the services of others." On one of my visits to his home, shortly before his death, I found him still actively engaged in assembling charts and reports on maternal statistics. During the last two years of his life he attended medical meetings in Virginia, Kentucky, Tennessee, Florida, and Texas. He also gave a postgraduate lecture in South Carolina. Incidentally, he drove his own car to all of these meetings.

Dr. Holmes at one time wrote an article entitled, "Names That Can Live"; I would like to write an article on "Names That Will Live" and place Dr. Rudolph Wieser Holmes at the head of the list.

4133 Manitou Way
Madison 5, Wis.

THE UNDERWEIGHT PATIENT AS AN INCREASED OBSTETRIC HAZARD*

WINSLOW T. TOMPKINS, M.D., DOROTHY G. WIEHL, M.A., AND ROBERT MCN. MITCHELL, M.D., PHILADELPHIA, PA.

(From the Pennsylvania Hospital [Philadelphia Lying-In Hospital] Nutrition Research Clinic†)

WITH the advent of antibiotic therapy and the availability of banked blood, the risk of death of the obstetric patient has been drastically reduced. Neither contribution, however, has markedly affected the hazard of the two greatest causes of maternal and infant catastrophe. Data relative to the metabolic and physiologic requirements of pregnancy have now become sufficiently definitive to preclude mere survival as a satisfactory criterion of adequate obstetric care.

The concept of the significance of nutrition and nutritional deficiencies in pregnancy recently published[1] pointed out that the various catastrophes of pregnancy are not separate clinical entities which can be expected to respond to some simple specific therapeutic agent. On the contrary, they were shown to be the result of complex, closely interrelated dysfunctions of the individual patient's metabolism and physiology; or, in brief, alterations in nutrition. Therefore, evidence which relates the nutritional status of an individual to the course and outcome of pregnancy, and thus to later catastrophes, is important in that it indicates an approach to these problems which can be preventive, rather than relying upon emergency symptomatic procedures after the catastrophe occurs.

Considerable objective evidence is available by which a patient's status can be evaluated relative to the anticipated stress to which she will be subjected during pregnancy. One extremely significant type of evidence, from a clinical point of view, is the weight of the patient at the time she becomes pregnant. This immediate pregravid weight is an objective observation reflecting the metabolic and physiologic efficiency within the patient. The increased risk of toxemia and other catastrophes to which the obese patient is subject has received a great deal of attention. From our studies at Philadelphia Lying-In Hospital, data for markedly underweight patients indicate that they, too, have a greater than average chance of toxemia and a greatly increased probability of premature labor.

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*Rudolph Wieser Holmes and Maria Baxter Holmes Lecture in memoriam to their mothers, presented at a meeting of the Chicago Gynecological Society on Nov. 20, 1953.

†The Nutrition Research Clinic is supported by grants-in-aid from the Milbank Memorial Fund, the Williams-Waterman Fund, the National Vitamin Foundation, the Upjohn Company, E. R. Squibb and Sons Company, in part by Mead Johnson & Company, and the Nutrition Foundation.

The relationship between immediate pregravid weight status* and toxemia among patients of the Nutrition Research Clinic† is shown in Fig. 1. It is obvious that patients who were 20 per cent or more overweight or underweight had an increased probability of developing toxemia. Differences in the rates are *not* statistically significant. The relatively high risk of toxemia for obese patients is generally known; the high risk for the extremely underweight patient suggested by these data needs further study on larger numbers of patients.

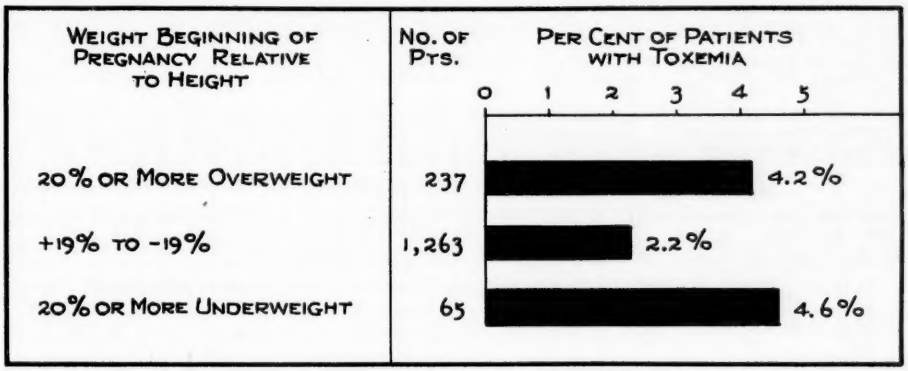

Fig. 1.—Incidence of toxemia among patients classified according to pregravid weight status.

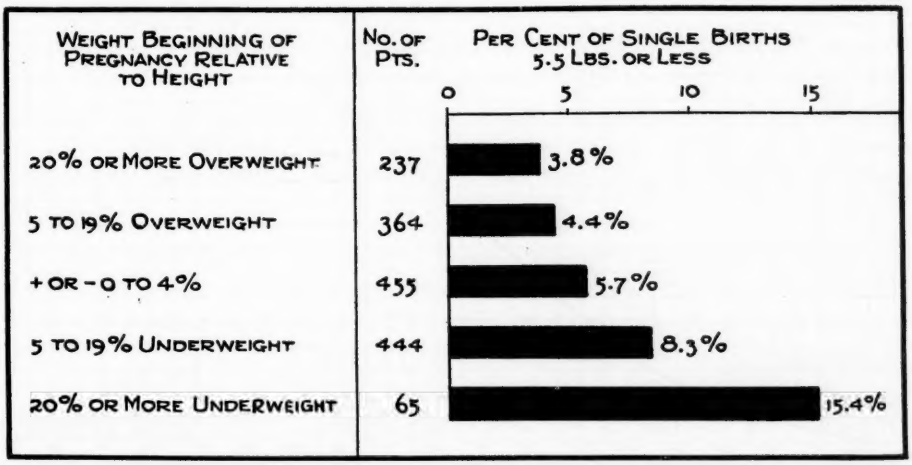

Fig. 2.—Incidence of premature births among patients classified according to pregravid weight status.

*The classification of patients according to their weight status at the beginning of pregnancy is based on standard tables of average weight for women of a given height at a specific age—not on weight alone. The average weight for height and age used is from the Report of the Medico-Actuarial Investigation 1912-1914; except that, at all ages over 25 years, the average weight at 25 years has been used as the standard or "ideal" weight in conformity with current attitudes concerning weight. This average, for ages 25 and over, is the midpoint of the weight range for women of medium frame published in the Statistical Bulletin of the Metropolitan Life Insurance Company, October, 1942. Patients were measured without shoes in the Nutrition Research Clinic, and an adjustment of one inch was made for height with shoes shown in published tables of height and weight. All patients were carefully questioned about their weight at the time their pregnancies began. Although some of the reported weights are undoubtedly in error a few pounds, and height alone is not always an adequate criterion for ideal or normal weight, groups of patients differing in their pregravid weight status may be compared to evaluate the effects of pregravid weight on the course and outcome of pregnancy.

†Patients were not included in this or other tabulations in this report who had heart disease Grade II-a or higher, essential hypertension, chronic kidney disease, or syphilis. In addition, only single births of at least 28 weeks' gestation are included.

In Fig. 2, immediate pregravid weight status is related to the occurrence of spontaneous premature labor, i.e., to the percentage of single births with a birth weight of 5.5 pounds or less. Here the clinical significance of the initial weight status of an individual in relation to the outcome of pregnancy is clearly indicated. The incidence of prematurity is lower for overweight patients than for those of approximately normal weight, and increases sharply for underweight patients. For all patients 5 per cent or more underweight, the rate for prematurity was 9.2 per cent compared with 4.8 per cent among patients overweight or of approximately normal weight; the difference between these percentages is highly significant ($P < .001$).

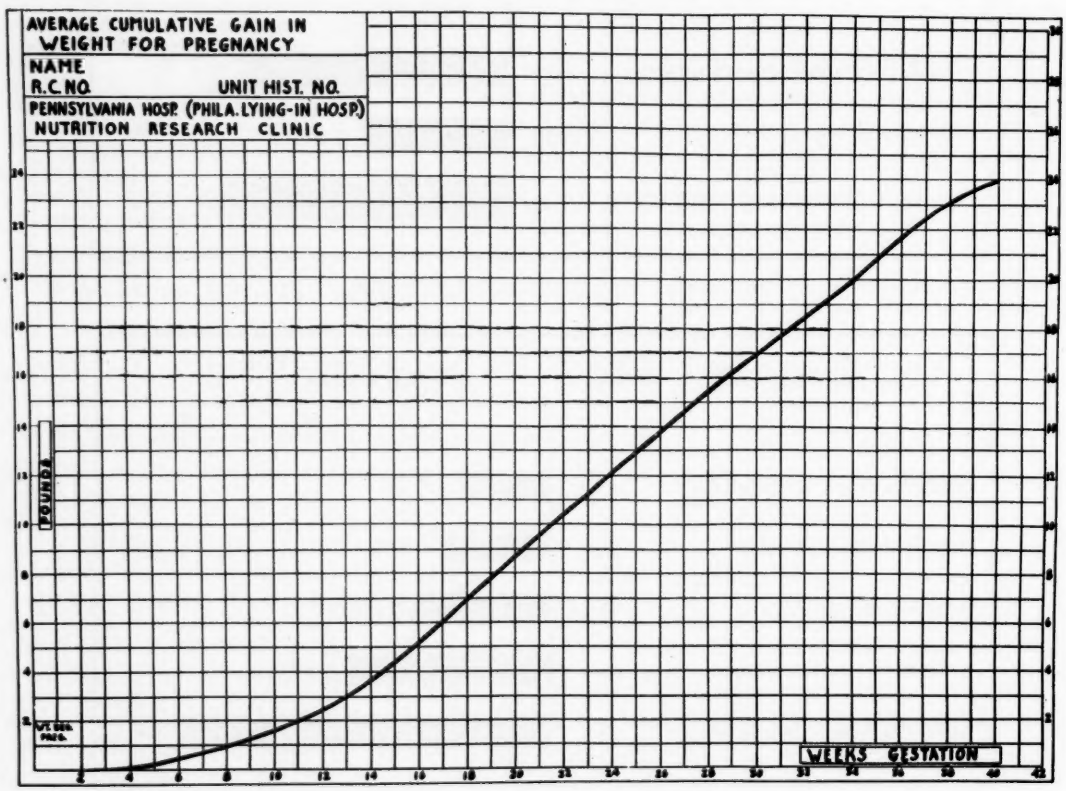

Fig. 3.—Average cumulative gain in weight during pregnancy for "normal" patients whose weight at beginning of pregnancy was within 10 per cent of standard weight.

Only weight at the beginning of pregnancy is considered in Figs. 1 and 2. For the underweight patients, weight changes during pregnancy and their relation to toxemia and premature labor are of clinical interest since, usually, it is only after pregnancy begins that the physician has an opportunity to influence the factors associated with changes in weight.

Gain in Weight in Pregnancy.—

Among the many changes occurring in pregnancy, the result of necessary alterations in metabolism and physiology, one of the most significant is the change in the patient's weight.

An analysis of our data for gain in weight of selected "normal" patients* resulted in a total average cumulative gain in weight during pregnancy of 24 pounds; 21 pounds from 13 weeks to 39 weeks. The cumulative curve by weeks is shown in Fig. 3.

The recommended change in weight during pregnancy, as generally stated, varies over such a wide range as to become fantastic. We believe that too much attention has been given to weight as a number, rather than to the objective evidence which an individual's weight at any specified time indicates relative to nutritional status. Unfortunately, there has been little factual or objective consideration of the marked and immediate metabolic needs, and the resultant physiologic changes, which predicate the alterations in weight which should be expected. It is particularly unfortunate that the first trimester of pregnancy has been essentially disregarded. It is during this period, the formative period, that the status of the fetus and the placenta is established. Although a "normal" pattern of gain in weight during the early weeks of pregnancy will not in itself guarantee protection to the patient and her infant, abnormal patterns do indicate probable later catastrophe if these early clinical warnings are disregarded.

Toxemia and Toxic Symptoms Among Underweight Patients Related to Gain in Weight.—

Among underweight patients the risk of toxemia was greater than average *only* for those who were excessively underweight, 20 per cent, or more. In this group of 65 patients, there were three with pre-eclampsia, too few for statistical interpretation of weight changes, but their prenatal gains in weight are suggestive that failure to gain in the first half of pregnancy is of probable significance.

The increased risk of developing toxic symptoms for underweight patients whose weight gains deviate much above or below the "normal" gain during the second trimester is evident in Table I. Furthermore, those who established a pattern of excessive gain which persisted through the third trimester had a very high probability of having toxic symptoms. It should be pointed out, however, that these very excessive gains are due, in part, to the edema which constitutes a major manifestation of metabolic and physiologic dysfunction for which the patient is placed in the toxic-symptom group. For these markedly underweight patients an excess gain of as much as 9 or 10 pounds at the end of pregnancy was compatible with a minimum risk of developing toxic symptoms.

Of equal clinical significance is the indication that *failure* to attain the average gain during the second trimester was associated with a relatively high probability of developing toxemia or toxic symptoms. Failure to gain weight should be considered an early warning of the patient's inefficient response to the increased metabolic and physiologic requirements of pregnancy.

*These patients were free of any major complications of pregnancy or toxic symptoms except for slight edema of the ankles noted once or twice for a few patients. All were within 10 per cent of the standard weight for height.

Premature Labor and Gain in Weight.—

The problem of prematurity is generally considered pediatric rather than obstetric; but, obviously, without premature labor there would not be a premature baby. Consequently, if a significant reduction in the greatest hazard to infant status is to be effected, objective and significant evidence is needed relative to this problem.

The significant relationship between the patient's weight status at the beginning of pregnancy and the frequency of premature births has already been discussed. Data on the weight gain during pregnancy of the underweight patients give evidence that this has an important relationship to the occurrence of premature labor.

TABLE I. PERCENTAGES WITH TOXEMIA OR TOXIC SYMPTOMS AMONG PATIENTS 20 PER CENT OR MORE UNDERWEIGHT, CLASSIFIED ACCORDING TO GAIN IN WEIGHT AT SPECIFIED PERIODS

DEVIATION OF WEIGHT GAIN FROM AVERAGE AT SPECIFIED PERIOD OF GESTATION	NUMBER OF PATIENTS			PERCENTAGE WITH TOXEMIA OR TOXIC SYMPTOMS
	TOTAL	WITH TOXEMIA	WITH TOXIC SYMPTOMS	
Total patients	65	3	10	20.0
12-16 weeks* to 24-26 weeks				
Above average 3-10 pounds	16	0	6	37.5
Average to 2 pounds above	24	2	0	8.3
Below average 1 to 5 pounds	25	1	4	20.0
12-16 weeks to maximum				
Above average 9-18 pounds.†	9	0	5	55.5
Average to 8 pounds above	28	2	1	10.7
Below average 1 to 9 pounds	28	1	4	17.9

*Gain is from 12-14 weeks except for 3 patients with first clinic visit at 15 weeks and 2 patients with first visit at 16 weeks. None of these had toxic symptoms.

†The 5 patients with toxic symptoms had an excess of 11 to 18 pounds and the other 4 had an excess of 9 or 10 pounds.

Gain in Weight During First and Second Trimesters.—

The influence on the premature labor rate of different patterns of gain in weight during the first and second trimesters of pregnancy by underweight patients and others has been studied for patients who registered with the Nutrition Research Clinic in its first three years, 1947 to 1949.[1] In Fig. 4, the striking relationship between gain in each of the first two trimesters and the rate of premature labor is shown for patients more than 5 per cent underweight at the beginning of pregnancy. When gain in the first three or four months was less than the average curve of gain, or there was loss in weight, the frequency of premature labor was more than twice that of the patients with average gain or more. Similar differences in the rates for prematurity are found between groups of patients with less than average gain, and average gain or more, in the second trimester. Of great importance clinically is the evidence that the underweight patient can be significantly protected if an average gain or greater is established early and maintained to the third trimester.

The significance of the pattern of gain in weight is further demonstrated in Fig. 5 which compares underweight patients with those who were of normal

weight or overweight at the beginning of pregnancy. For both groups, premature births were nearly three times as frequent among the patients who gained *less* than average from the first visit to the clinic to the end of the second trimester, as among the patients who had the average gain or greater.

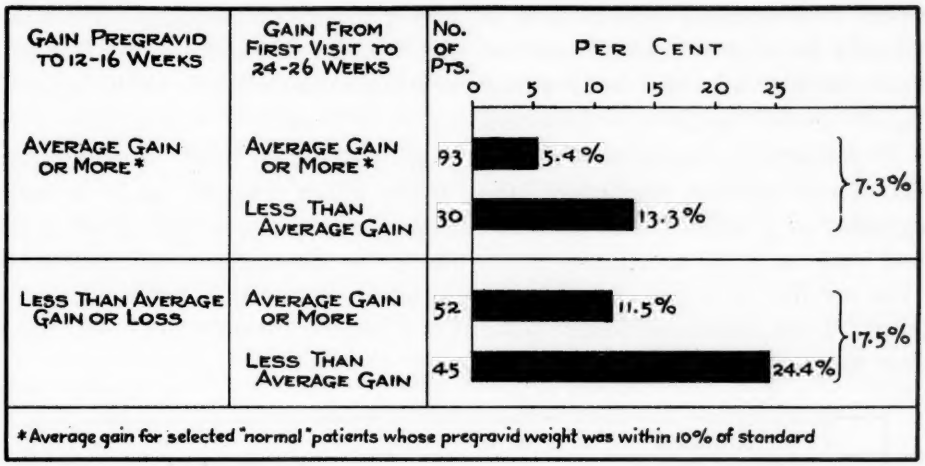

Fig. 4.—Incidence of premature births in relation to gain in weight during the first and second trimesters for patients more than 5 per cent underweight at beginning of pregnancy.

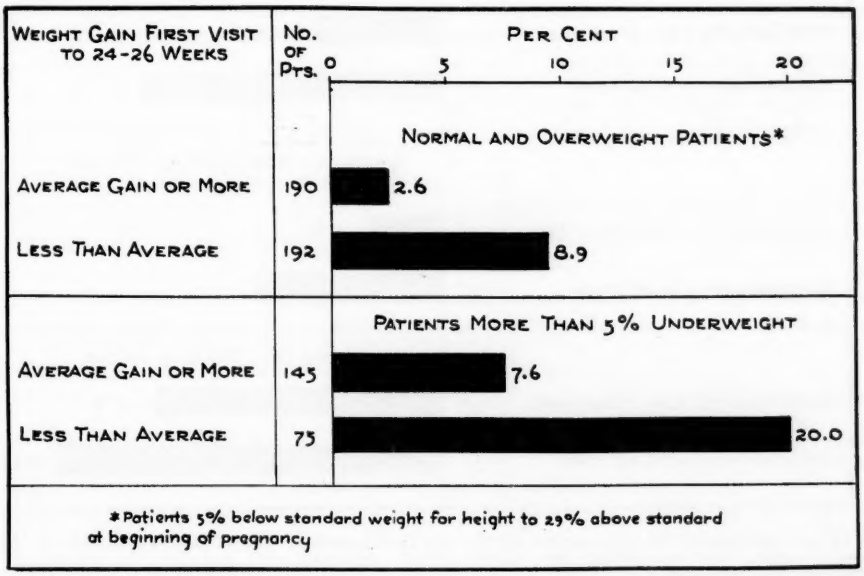

Fig. 5.—Incidence of premature births in relation to gain in weight in the second trimester for underweight patients and for normal and overweight patients.

The increased hazard of premature labor for underweight patients is very apparent. But, for all patients, it is clear that early stabilization of the patient with a steady gain in weight at the average rate could contribute significantly to a reduction in premature labor which is the highest single cause of infant loss.

The individual markedly underweight is obviously not obtaining a sufficient quantity of nutrient intake to maintain standard body weight, and is certainly lacking in the essential nutrients necessary for the support of normal body function. It is good reason to assume that if adequate nutrition is necessary for the maintenance of nonpregnant normal body function, the successful support of pregnancy will require an added intake of essential nutrients. It is equally good reason to assume that this increase in essential nutrient intake cannot begin at a period in pregnancy when a catastrophe is about to occur if adequate protection is to be obtained.

If remedial procedures are to be instituted in an effort to preclude the onset of spontaneous premature labor, every effort must be made as early in pregnancy as possible. The pattern for spontaneous premature labor is established very early in pregnancy, particularly for the underweight patient, and by the middle or latter part of the second trimester this pattern cannot be altered. Thus, the underweight patient is a hazard not only to herself but also to her baby.

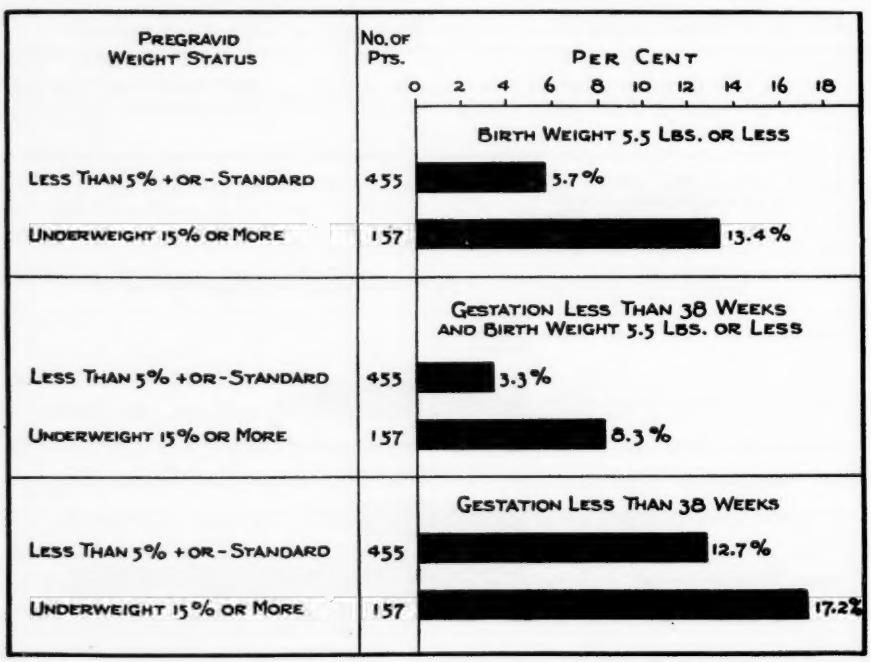

Fig. 6.—Incidence of premature births on the basis of birth weight, length of gestation, and both weight and gestation for underweight patients and patients of "normal" weight at beginning of pregnancy.

Prematurity by Length of Gestation

The standard for prematurity in the preceding analysis has been birth weight alone in accord with accepted practice. The length of gestation cannot be estimated accurately due to errors in reporting the date of the last menstrual period and variations in time of conception. Some indications, however, of the relative maturity of small babies born to underweight patients,

and to those of normal pregravid weight, is of clinical importance with respect to both the patient and the infant. Therefore, both birth weight and duration of gestation are considered in Fig. 6, which gives a comparison of patients of approximately standard weight with patients 15 per cent or more underweight.

The lower section of Fig. 6 shows that only a small, and not significantly larger, percentage of births with an estimated gestation period of less than 38 weeks occurred among the underweight patients. If the percentages on the basis of length of gestation alone are compared with those in the middle section of Fig. 6 for gestation and birth weight, it is evident that for both groups the majority of babies with an estimated gestation period of less than 38 weeks weighed more than 5.5 pounds. Some of these probably were immature, but in most instances the gestation period undoubtedly is erroneous.

Both among underweight patients and among those of standard weight, however, approximately 60 per cent of the babies that weighed 5.5 pounds or less at birth had an estimated length of gestation of less than 38 weeks. Thus, on the basis of both criteria, the underweight patients had a greater risk of premature labor. The rate for premature labor among the patients 15 per cent or more underweight is more than twice the rate* among patients of standard weight whether weight alone is the criterion or weight and length of gestation.

Prenatal Gain in Weight and Size of Baby

It has been shown that average or greater gain in weight by underweight patients reduced the percentage of babies that weighed 5.5 pounds or less at birth. Thus, it is of interest to examine the effect of weight status of the mother at the beginning of pregnancy and her prenatal gain in weight on the weight and size of all babies.

The average weight of babies born to patients who were 20 per cent or more underweight at the beginning of pregnancy is about 11 ounces less than

TABLE II. AVERAGE BIRTH WEIGHT AND AVERAGE CROWN-SOLE LENGTH OF BABIES AND AVERAGE HEIGHT OF MOTHERS FOR MOTHERS WHOSE WEIGHT AT BEGINNING OF PREGNANCY WAS WITHIN 5 PER CENT OF STANDARD WEIGHT AND THOSE 20 PER CENT OR MORE UNDERWEIGHT

MEASUREMENT AND PREGRAVID WEIGHT STATUS OF MOTHER	NUMBER	AVERAGE	STANDARD ERROR OF AVERAGE	SIGNIFICANCE OF DIFFERENCE
*Birth Weight.**—				
Mother standard weight	440	7.37	.046	
Mother underweight 20%+	60	6.69	.134	$P < .001$
*Crown-Sole Length of Baby.**—				
Mother standard weight	379	49.85	.108	
Mother underweight 20%+	50	48.43	.271	$P < .001$
Height of Mother.—				
Mother standard weight	455	62.0	.115	Not significant
Mother underweight 20%+	65	61.9	.324	

*Excludes babies of less than 38 weeks of gestation with birth weight of 5.5 pounds or less.

*By weight alone the difference between the percentages of premature babies among underweight and standard-weight patients has a statistical probability of less than 1 per cent; by weight and gestation, probability of the difference is approximately 1 per cent.

the average weight of babies of patients of standard weight. As shown in Table II, the averages were 6.69 pounds and 7.37 pounds.

This difference in weight at birth is due to a statistically significant difference in the length of the babies, and is not the result of greater amounts of soft tissue relative to skeletal size. Most of the babies were measured at one to five days after birth, and the average crown-sole lengths are shown in Table II. Babies of patients in the underweight group were, on the average, more than 1 cm. shorter.

The patients in each of these weight status groups did *not* differ in height. The average height of those in the standard weight group was 62.0 inches, and for the patients 20 per cent or more underweight the average was 61.9 inches. Thus, although the length of the baby at birth may be affected to some degree by genetic factors, it appears that the weight status of the mother is a dominant factor affecting fetal growth.

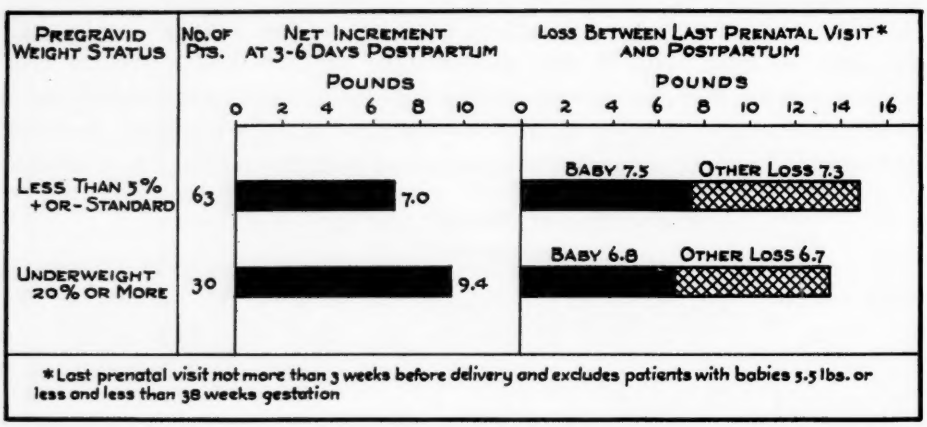
Pregravid Weight Status
No. of Pts.
Net Increment at 3-6 Days Postpartum
Pounds
0 2 4 6 8 10
Loss Between Last Prenatal Visit* and Postpartum
Pounds
0 2 4 6 8 10 12 14 16
Less Than 5% + or - Standard
63
7.0
Baby 7.5
Other Loss 7.3
Underweight 20% or More
30
9.4
Baby 6.8
Other Loss 6.7
*Last prenatal visit not more than 3 weeks before delivery and excludes patients with babies 5.5 lbs. or less and less than 38 weeks gestation

Fig. 7.—Average net gain over pregravid weight after delivery and average loss in weight at delivery for underweight and "normal" weight patients at beginning of pregnancy.

These differences in weight and skeletal length of babies of patients who differed widely in immediate pregravid weight status raise the question as to the relationship of the prenatal gain in weight to the size of the baby. In order to eliminate, as far as possible, the effect of edema on the recorded gain in weight, the comparison of prenatal gain in weight is based on selected "normal"* patients in each group. In addition, only patients are included for whom a record of postpartum weight three to six days after delivery was available. The postpartum weight makes it possible to separate the total cumulative gain in weight into three categories: the baby's weight, other weight loss at delivery which includes placenta, amniotic fluid, and plasma volume change; and also the net increment of tissue mass added to the patient's body weight.

In Fig. 7, the average amount of gain in weight identified with each of the three categories is shown for "normal" patients in the underweight group and the standard-weight group.

*Patients selected as "normal" did not have prenatal complications, toxemia, or edema, except slight ankle edema one or two times for a very few patients; and none had premature babies by weight and gestation.

These data show a total average gain to the last prenatal visit over the pregravid weight of 22.9 pounds by the underweight patients, and 21.8 pounds by the patients of standard weight. Thus, the gain was slightly greater for underweight patients. The average weight of the babies of these selected patients, however, differed in about the same amount as for the total groups; that is, the babies of underweight patients averaged 0.7 pounds less than those of the patients of standard weight.

It is notable that the very underweight patients had a greater net body increment in weight after delivery. Under the stimulus of an increased metabolic rate during pregnancy, the underweight patient apparently adds to her own active tissue mass at some sacrifice to the fetus. Consequently, there is no indication that a relatively high rate of gain by underweight mothers does increase the size of the baby. The increase in her own tissue mass may afford greater protection to meet the stress of pregnancy.

It may be concluded that the strong association between the size of the baby and pregravid weight status of the mother operates independently of prenatal gain. Failure to gain an average amount, especially in the first two trimesters, increases the likelihood of premature labor, but greater gain has little, if any, effect on the size of the baby.

Summary

Evidence has been presented that adequate nutrition and nutritional deficiencies play a critical role in our effort to reduce maternal and fetal catastrophe.

Both the obese and the excessively underweight patient have an increased hazard of toxemia.

Premature labor is inversely associated with the immediate pregravid weight status of the patient, being lowest among overweight patients and increasing sharply for underweight patients.

Among patients 20 per cent or more underweight the occurrence of toxemia or toxic symptoms increased for those who *failed* to gain an average amount before the third trimester as well as among those who gained excessively.

The hazard of premature labor for underweight patients is much higher if the gain in weight is less than the average gain in the first or second trimester, and is significantly reduced if an average or greater rate of gain is established during the second trimester.

Babies of underweight mothers are significantly lighter and shorter than babies of mothers of approximately standard weight at the beginning of pregnancy.

Underweight patients tend to add more to their own body tissue mass during pregnancy than patients of standard weight, and apparently at the sacrifice of the fetus.

Reference

1. Lull, C. B., and Kimbrough, R. A., Jr.: Clinical Obstetrics, Philadelphia, 1953, J. B. Lippincott Company, chap. 9.

NISENTIL—AN OBSTETRIC ANALGESIC*

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THE introduction of any new analgesic agent raises the question as to its applicability as an agent for obstetric use. Nisentil† (1,3-dimethyl-4-phenyl-4-propionoxy-piperidine hydrochloride [dl-alpha form]) has certain qualities which should make it useful for predelivery analgesia; the most important of these are the rapidity with which it acts and the relatively short duration of the effect. Pharmacological data suggest that it has about the same analgesic potency as morphine and Demerol. Smith and Nagyfy[1] in 1949 reported that in doses of 30 mg. or less it compared favorably with other drugs used in their study. Hapke and Barnes[2] found that in over 90 per cent of their intrapartum patients 40 mg. of Nisentil provided adequate analgesia. Kane[3] reported that doses of 60 mg. gave satisfactory analgesia for 98.1 per cent of deliveries.

The present study was undertaken to evaluate the effectiveness of Nisentil in producing pain relief during normal labor. The results were judged both on the basis of objective observations of the patients during labor and their subjective reactions as determined by questioning them and recording their comments during the first 24 hours after delivery. The patients selected for the study were at or near term; all had had an uneventful prenatal course and none had either a medical or an obstetric complication.

When labor was established, 40 mg. of the drug was administered subcutaneously either alone or in combination with 0.4 mg. or 0.6 mg. of scopolamine to 378 primigravidas and 622 multiparous patients delivered in the Temple University Hospital. In no instance was a barbituric acid derivative or another analgesic agent used. A single dose was administered to 834 patients, while in the remaining 166 the medication was repeated at least once; 3 patients received the drug four times. The usual labor supervision was carried out, the duration of contractions, maternal blood pressure, and fetal heart tones being recorded at regular intervals. The objective observations were made by the author and members of the obstetric division and were recorded as no appreciable effect, slight, moderate, or marked pain relief.

Results

Effectiveness—Objective.—

There were no side effects noted which could be directly attributed to Nisentil. The nystagmus reported by Hapke and Barnes[2] was not noted.

*Presented at a meeting of the Obstetrical Society of Philadelphia, Nov. 5, 1953.
†Supplied by Hoffman-La Roche, Inc., Nutley, N. J.

The patients were observed after administration of the medication for signs of drowsiness and increased pain tolerance. The average time of the first noted effect was 11 minutes, the range being from 5 to 30 minutes. In 229 the effect was noted within 5 minutes, in 384 within 10 minutes, in 198 within 15 minutes, in 95 within 20 minutes, while in only 9 patients the time noted was approximately 30 minutes; in 77 the time of onset was unknown. In 92 patients no appreciable analgesic effect was noted. The drug appears to be equally effective in both primigravidas and multiparous patients; the analgesic effect, however, was somewhat more profound in the patients who were experiencing the discomfort of labor for the first time than in those with memories of other agents. The most probable explanation for this seeming disparity is the shortness of the multiparous labor; in many instances the full effect was not evidenced by the time of delivery. Scopolamine did not alter the time of onset of analgesia, the duration of pain relief, or the apparent effectiveness of Nisentil. Subsequent doses of the same drug were not given to the 92 patients in whom the initial dose produced no effect for this would have distorted the results; where time permitted such patients were given some other agent. There is a greater degree of effectiveness when the period of time between the administration of the drug and the actual delivery is over 30 minutes. The average observed duration of analgesia was 107 minutes, the range being from 70 to 120 minutes. The data suggest that the more effective the drug the longer the duration of its action.

At the completion of the second stage of labor 976 patients were given an anesthetic agent, the majority of deliveries being consummated under regional anesthesia.

Effectiveness—Subjective.—

Of the total group surveyed, 831 considered this a satisfactory agent, 67 were dissatisfied, and 102 were not sure that they had obtained the degree of pain relief that they desired. It is interesting to note that of the group in whom no objective analgesic effect was observed, 2 considered their relief adequate and 57 were not sure that satisfactory pain relief had been obtained (Table I).

TABLE I. EFFECTIVENESS, SUBJECTIVE AND OBJECTIVE

SUBJECTIVE RESPONSE	OBJECTIVE RESPONSE*				TOTAL
	0	1	2	3	
Satisfactory	2	29	464	336	831
Unsatisfactory	33	31	0	3	67
Questionable pain relief	57	32	10	3	102
Total	92	92	474	342	1,000

*0—No appreciable effect, 1—slight relief, 2—moderate relief, 3—marked relief.

Effect on Uterine Contractions.—

The observed effect on uterine contraction patterns was interesting. In 96 patients some change was noted; this was not related to parity. LaForge[4] reported that no harmful interference with the mechanism of labor was noted,

but in 83 women in this survey the interval between contractions became longer and the duration became shorter, the over-all effect being apparently to interfere with the mechanism of labor. In 5 patients contractions could no longer be palpated within 10 minutes after administration of Nisentil and were only resumed 90 minutes later. In the remaining 8 a questionable uterine effect with irregularity of the interval between and the duration of the contractions was noted. All of these patients had a marked objective response. The most probable explanation for these findings is that the drug was administered too early in labor.

TABLE II. EFFECT ON UTERINE CONTRACTIONS—OBJECTIVE

CONTRACTIONS	NO. OF CASES
Slowed	83
Stopped	5
Questionable	8
Total	96

At no time was there noted a significant change in the maternal blood pressure or the fetal heart tones.

Effect on the Infant.—

There were no neonatal deaths though there were 3 stillbirths in the total of 1,000 deliveries, but none was thought to be attributable to Nisentil, the intrauterine fetal deaths having been diagnosed prior to the administration of the drug. In 162 patients sedation was given less than 45 minutes prior to delivery without demonstrable effect on the initiation of respiration in the baby; 28 of this group received medication within 15 minutes of delivery. This is consistent with the finding of Hapke and Barnes[2] though the time is less than their reported sixty-minute interval between sedation and delivery. Nine infants, 0.9 per cent, manifested respiratory difficulties after delivery. In each instance a drop in fetal heart tones had been noted prior to delivery so that it was difficult to indict Nisentil as the causative factor. In one a single injection of the drug had been given 53 minutes before delivery, in 5 others single doses had been administered between 68 and 120 minutes before delivery, and in the remaining 3 at least 210 minutes had elapsed between the use of Nisentil and the birth of the baby.

Conclusions

1. Nisentil in a dose of 40 mg. has been surveyed in a group of 1,000 women during labor and was found to provide satisfactory analgesia in approximately 92 per cent.

2. There was no discernible effect upon the initiation of respirations in the newborn, though respiratory depression was noted in 0.9 per cent of the infants.

3. Disturbance of a supposedly normal mechanism of labor as evidenced by a decrease in frequency and duration of uterine contractions was noted in 9.6 per cent of the patients.

4. On the basis of this study Nisentil appears to be a suitable agent for use during labor because of the rapid onset of its action, the lack of maternal side effects, and the freedom of interference with respirations in the newborn. These factors plus the duration of action make the drug especially advantageous for use in the multiparous patient.

I wish to thank Dr. J. Robert Willson for his helpful suggestions and criticisms and the residents of the Temple University Hospital for their help in collecting the data.

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PUDENDAL BLOCK ANESTHESIA FOR ROUTINE USE*†

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FOR many years an anesthetic that offers minimal risk to mother and child has been sought by the obstetrician. The perfect anesthesia for routine use has not as yet been found, but by judicious selection the prudent physician is able to choose from the large armamentarium an anesthetic which satisfactorily meets the needs of the obstetrician and the desire and welfare of the mother and her baby.

This study was undertaken in quest of an anesthetic for routine use on a ward obstetrical service of an Armed Forces hospital. Because of frequently changing and variously trained medical officers, the obstetric anesthesia, to be satisfactory, must be safe as well as simple of administration without the services of a trained anesthetist.

Hingson and Hellman[1] believe that maternal deaths resulting from, or related to, anesthesia are in fifth place after heart disease as a contributor to obstetrical mortality. Aspiration of vomitus accounted for 155 fatalities in their study of 330 deaths due to anesthesia; overdosage of spinal anesthetics was incriminated in 24 deaths. Greenhill,[2] in editorial comment on this article, states: "Three hundred and thirty deaths from anesthesia for a natural process is far too great a penalty to pay for relief from pain." Greenhill[3, 4, 5] has long propounded the dangers of spinal anesthesia in obstetrics and believes that it is definitely contraindicated when an anesthesiologist is not available. He feels that, as parturition is a normal physiological process, there is no justification for subjecting the parturient to undue risk and strongly advocates the use of local infiltration or pudendal block anesthesia, "the safest of all anesthetics in obstetrics."

Inhalation anesthesia in obstetrics[6] has been in use for many years and where an anesthesiologist is available has been satisfactory for the needs of the obstetrician, and the welfare of the mother and her baby. Improper or careless administration of these agents, however, constitutes a serious hazard.

Pudendal block has been in limited use for more than four decades. Consideration of its minimal risk to mother and child, and the rarity of contraindications to its use appear to make it the ideal anesthetic; in practice, however, considerable experience in its administration is required and anesthesia

*This work is not to be construed as necessarily reflecting the views or the endorsement of the Department of the Navy.

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may develop too slowly to be satisfactory, particularly when the second stage of labor is rapid. The recent introduction of hyaluronidase and epinephrine as adjuvants in pudendal block has overcome the main objections to this method in that the spreading factor and penetrating effects of these drugs when used with procaine produce a rapid and lasting anesthesia when the anesthetic solution is deposited in the proximity of the nerve trunk. The mode of action and technique of administration have been adequately described by many investigators[7-11] and will not be taken up here.

Material

This report is a study of 700 cases of pudendal block using 1 per cent procaine with hyaluronidase and epinephrine. During the period from Sept. 1, 1951, to March 1, 1953, pudendal block has been the most commonly employed anesthetic for vaginal deliveries on the Obstetrical Service of the U. S. Naval Hospital, Memphis, Tennessee. During this period there were 1,709 consecutive deliveries of which 1,054, or 62 per cent, were conducted under pudendal anesthesia. The gross infant mortality for this period was 2.93 per cent, the maternal mortality was zero, and the maternal morbidity 3.22 per cent. The use of pudendal block anesthesia has been indicated by reasons of safety and simplicity, as well as by the fact that the routine services of a trained anesthetist are not available. The cases were completely unselected ward cases and the only criterion for their inclusion was that the objective and subjective data sheets in each case should be completed in their entirety.

Other types of anesthesia were administered, where indicated, by choice of the operator or in deference to the patient's wishes, and included ether as a supplement to failed pudendal block and local infiltration, local infiltration with procaine, drop ether, nitrous oxide-oxygen-ether (G.O.E.), saddle block, spinal for some cesarean sections, and, since December of 1952, trichlorethylene (Trilene) either alone or in conjunction with local infiltration or pudendal block (Table I).

TABLE I. ANESTHETICS ADMINISTERED SEPT. 1, 1951, TO MARCH 1, 1953
(1,709 DELIVERIES)

	PUDENDAL	LOCAL	NONE	PUDENDAL AND TRILENE	TRILENE	DROP ETHER	PUDENDAL AND ETHER	SADDLE BLOCK	G.O.E.	LOCAL AND ETHER	SPINAL
No. of cases	1,002	184	177	77	62	53	52	38	27	24	13
Per cent	58.6	10.8	10.4	4.5	3.6	3.1	3.0	2.2	1.6	1.4	0.8

In order to interpret properly the results in this series it is necessary to understand the conditions under which these blocks were performed. The entire series was carried out over a period of eighteen months by twenty-eight medical officers, only four of whom had had specialty training in obstetrics. The majority of these doctors were assigned to obstetrics for only a short period of time and included general practitioners, pediatricians, obstetricians, and several doctors who had just completed internship. It is felt that the element of specialization was minimized and that the series is comparable to what might be expected in the general employment of pudendal block by physicians without specialty training in obstetrics or anesthesia.

Method of Study

Each of the 700 patients was delivered under pudendal block anesthesia. As soon as practicable after the delivery the operator completed an objective study sheet which included his observations of the course of labor, the effects and efficiency of the analgesia and anesthesia, need for resuscitation of the newborn, supplemental anesthesia required, maternal blood loss, evaluation of perineal relaxation during delivery, presence or absence of edema and bleeding in the perineal tissues, and general comment on the result of the block. In addition, pertinent obstetrical data were recorded.

Within forty-eight hours after delivery each patient was interviewed and the subjective study sheet was completed. The questions are the same as those used in a study of pudendal block by Taylor and Jack.[12] These questions were as follows:

1. How do you feel?
2. Do you remember your baby being born?
3. Did you have much pain in labor?
4. Do you remember going to the delivery room?
5. Did you have pain when the baby was born?
6. Did you have pain in the delivery room?
7. Did you feel better after the "shots"?
8. If you were to have another baby, would you want the shots?
9. What anesthetic did you have with your last baby?
10. Which anesthetic do you prefer?

The subjective interviews were conducted by two specialists in obstetrics and every effort was made to obtain frank and accurate answers.

Technique of Analgesia and Anesthesia

It was routine for all patients to receive 100 mg. (1½ grains) of Seconal or Nembutal on admission to the hospital unless delivery was imminent. When labor was definitely established and the pains were becoming uncomfortable, that is, when a cervical dilatation of 3 to 4 cm. was reached in primiparas, or when uterine contractions were regular with progressive dilatation of the cervix and descent of the presenting part in a multipara, Demerol, 100 mg. (1½ grains), and scopolamine, 0.65 mg. (1/100 grain), were administered intramuscularly. The Demerol was repeated in 50 or 100 mg. doses every 4 to 6 hours with one-half the original amount of scopolamine. When the patient was ready for delivery and after draping and perineal preparation, the pudendal block was administered. The anesthetic solution used in this study consisted of 30 c.c. of 1 per cent procaine with 150 turbidity-reducing units of hyaluronidase and 0.25 to 0.5 c.c. of epinephrine. The technique of administration as described by Heins[8] was used.

The majority of maternity patients seen in an Armed Forces hospital are in the younger age group, 66 per cent being primigravidas and 34 per cent multigravidas in this series. In the 700 cases, there were 97 per cent vertex presentations and 3 per cent breech. Eleven forceps rotations of posterior position were done satisfactorily under pudendal block as were 4 applications of Piper forceps to the aftercoming head. Episiotomies and repairs were done in 82 per cent of the patients, and 93 per cent received Demerol-scopolamine analgesia. Eighteen cases of postpartum hemorrhage occurred. There was hematoma formation in 2 cases, one in the rectovaginal septum and one in the labia majora, both extending from the episiotomy. There were 5 cases of episiotomy breakdown, none of which required secondary suture. Two cases

of methemoglobinemia occurred, caused by accidental contamination of the anesthetic solution with sodium nitrite. There were no cases of infection of the perineal area. Eighteen babies required resuscitation (Table II).

TABLE II. DATA ON 700 CASES OF PUDENDAL BLOCK

	NO. OF CASES			PER CENT
Parity:				
Primigravidas	463			66.1
Multigravidas	237			33.9
Type of delivery:				
Vertex	681			97.3
Spontaneous		406		58.0
Low forceps		275		39.3
Forceps rotation			11	
Breech	19			2.7
Spontaneous or assisted		15		
Piper forceps		4		
Episiotomies	570			81.5
Analgesia:				
Demerol and scopolamine	653			93.3
None	47			6.7
Maternal complications:				
Hemorrhage, post partum	18			2.6
Hematoma formation	2			0.3
Episiotomy breakdown	5			0.7
Methemoglobinemia*	2			0.3
Infection, perineum	0			
Resuscitation of newborn	18			2.6

*To be reported later.

It was noted that within five to ten minutes after the injection of the procaine-hyaluronidase-epinephrine mixture there was a noticeable epinephrine effect upon the uterine contractions. As a rule the uterine contractions stopped for a variable period of from 10 to 20 minutes after which they resumed their previous strength and frequency. In some instances the only effect was a transitory decrease in the strength and frequency of contractions. It was sometimes necessary to infiltrate the perineum for the completion of the repair, most often when an hour or more had elapsed from the time of original nerve block.

An ideal anesthetic may be defined as one with which the operative procedure is completed without pain or discomfort to the patient. A satisfactory anesthesia is then one in which the indicated procedure is completed with only slight discomfort, and a failure is a case where the local anesthesia has to be abandoned or supplemented with inhalation anesthesia. With the use of these criteria,[8] the results in this series as appraised by the operators are shown in Table III.

TABLE III. OBJECTIVE APPRAISAL OF RESULTS

	NO. OF CASES	PER CENT
Ideal	249	35.6
Satisfactory	358	51.1
Failure	93	13.3

When compared with a similar series given by Heins[8] of the Medical College of the State of South Carolina and another series of local anesthetics reported by Buxbaum[13] from the Chicago Maternity Center it is felt that this series, taking into account the lack of specialty training by the majority of the operators, compares favorably (Table IV).

TABLE IV. HEINS' AND BUXBAUM'S SERIES

FINAL END RESULT	HEINS SERIES	BUXBAUM SERIES
Ideal	160 (80%)	880 (40%)
Satisfactory	30 (15%)	1,410 (55%)
Failure	10 (5%)	110 (5%)

A study of the subjective data sheets reveals interesting conclusions on the part of the patient (Table V). Twenty-five per cent (172) of the patients did not remember being transferred to the delivery room and 24 per cent (165) did not remember their babies being born; 41 per cent (289) reported that they did not experience much pain in labor and 62 per cent (437) had no pain when the baby was born; 18 per cent (125) reported mild pain only when the baby was born. Ninety per cent (630) stated that they desired the analgesia for future deliveries. Of the 463 primigravidas 85 per cent (394) stated that they desired pudendal block for future deliveries. Of the multigravidas, 76 per cent (180) stated a preference for pudendal block. The anesthesia preference of the 126 patients not desiring pudendal block for future deliveries is shown in Table V.

TABLE V. TABULATION OF SUBJECTIVE DATA

	NO. OF CASES	PER CENT
Remember baby being born	535	76.4
Considerable pain in labor	411	58.7
Remember transfer to delivery room	528	75.4
Felt pain when baby born	138	19.7
Felt mild pain when baby born	125	17.9
Felt no pain when baby born	437	62.4
Felt pain in delivery room	167	23.9
Felt mild pain in delivery room	139	19.9
Felt no pain in delivery room	394	56.2
Pain relieved by Demerol and scopolamine	618	88.3
Desire Demerol and scopolamine for future deliveries	630	90.0
Anesthetic preferred for future deliveries		
Pudendal	574	82.0
Primigravidas 394 (85%)		
Multigravidas 180 (76%)		
Ether	70	10.0
Spinal	35	5.0
Gas	20	2.8
Caudal	1	0.2

The patients rated pudendal block as satisfactory in 95 per cent (662) of the cases and as unsatisfactory in 5 per cent.

TABLE VI. SUBJECTIVE APPRAISAL OF PUDENDAL

	NO. OF CASES	PER CENT
Excellent (patient satisfied)	236	33.7
Good (patient satisfied)	426	60.9
Failure (not satisfactory)	38	5.4

Comment

From the standpoint of providing an effective, safe, simple-to-administer second-stage anesthetic for childbirth, pudendal block with hyaluronidase and epinephrine has proved itself to be closer to the ideal anesthetic for ward use by practitioners who are not specialists in the fields of obstetrics or anesthesiology than any of the other methods currently in use. As far as can be determined, there is no risk to the mother or infant and there are no contraindications to its use for uncomplicated vaginal delivery. Delivery by low forceps, manual and forceps rotation, spontaneous and assisted breech, and episiotomy and repair were done without undue discomfort to 95 per cent of the patients.

The duration of anesthesia is sufficient for the average uncomplicated delivery. Additional infiltration was required for the repair in some cases. Excessive bleeding and edema of the perineal tissues attributable to this method were not encountered.

The results in this series tend to corroborate Heins'[7] observation that infiltration of the anesthetic mixture in the vicinity of the pudendal nerve produces an effective block. A much higher incidence of successful blocks performed by a large number of individuals was obtained than has previously been reported with the use of procaine alone as the anesthetic, even in experienced hands.

The temporary cessation or slowing of uterine contractions following administration of the anesthetic is a constant observation and is attributed to the epinephrine effect. The short delay caused by this effect was not considered of importance but it is considered advisable that recognition be given this period of uterine inertia in order to avoid hemorrhage caused by detaching the placenta before uterine tone returns.

The administration of Demerol-scopolamine analgesia is considered an important adjunct to the success of the pudendal block as judged by the patient. The occasional occurrence of excitement is considered a disadvantage from the standpoint of the operator but is outweighed by the analgesia and amnesia afforded the parturient.

Conclusions

1. The use of a procaine-hyaluronidase-epinephrine mixture for pudendal block anesthesia in the second and third stages of labor was studied in 700 unselected deliveries.

2. Anesthesia was regarded by the patient as being satisfactory in 95 per cent of the cases and was satisfactory from the doctor's standpoint in 87 per cent of the cases.

3. There is no systemic effect on the mother or infant.

4. The duration of anesthesia is sufficient for normal delivery.

5. The spreading property of hyaluronidase makes deposition of the anesthetic directly at the site of the nerve unnecessary.

6. Demerol-scopolamine analgesia is a valuable adjunct to pudendal block.

7. Pudendal block with hyaluronidase and epinephrine is a near-ideal obstetrical anesthetic for routine use on ward service, and is recommended as a simple, safe, and effective anesthesia. In the hands of doctors not ordinarily practicing obstetrics, it is of special value.

Addendum

Since this study was completed, pudendal block anesthesia with the substitution of Xylocaine for the procaine-hyaluronidase-epinephrine mixture has been administered in additional cases with highly satisfactory results. The Xylocaine has good spreading properties and the temporary cessation or slowing of uterine contractions attributed to the epinephrine of the original anesthetic mixture has not been observed.

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THE EFFECT OF NEEDLE SIZE ON THE INCIDENCE OF POSTDELIVERY SPINAL HEADACHE*†

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ANESTHESIA for the obstetric patient continues to present challenging problems as evidenced by the fact that there is no method which is universally considered as standard. The safest forms of anesthesia by and large offer a lower incidence of complete relief from pain than do those which are more complicated and possibly more dangerous. In this latter group we would certainly include the intrathecal techniques.

The number of headaches due to spinal anesthesia as well as other minor and some more serious complications have led many physicians to abandon its use completely, despite the fact that it frequently offers definite advantages over other methods for pain relief. The reported incidence of this complication ranges from 0.4 to 26 per cent with the usual techniques for dural punctures and injections (Table I).

TABLE I. REPORTED INCIDENCE OF HEADACHE FOLLOWING USE OF NEEDLES OF DIFFERENT SIZES

REPORTER	NO. OF CASES	SIZE OF NEEDLE	% HEADACHES
1. Lewis and Austin	1,032	19	9.1
2. Ahearn and Huston	400	20 22	19.5
3. Hanahan and Redding	388	20	13.9
4. Haugen and Benson	1,000	20 22	6.3
5. Weintraub and Antine	300	18 22	15.0
6. Andros, Dieckmann, et al.	719	—	14.5
7. Cosgrove	2,789	—	17.0
8. Greene, B. A., et al.	120	24	2.5
9. Greene, B. A.	700	24	0.4

Many drugs have been used to relieve or reduce the severity of the headache, but as yet none has given consistently satisfactory results. Therefore, it appears more practicable to attempt to acquire a better understanding of its cause and to direct our efforts toward preventing its occurrence.

Pathogenesis.—In reviewing the literature one finds that the most widely held viewpoint is centered about a cerebrospinal leakage through the puncture opening in the dura which can persist for a variable number of days. The

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leakage is followed by a reduction in the volume and in pressure within the cerebrospinal canal. This in turn leads to compensatory dilatation of the intracranial vessels and when the patient assumes an upright position, to traction on the anchoring structures of the brain, the stimulus directly causative of the headache.

It has been proved conclusively that a lower cerebrospinal fluid pressure is present in those patients with headaches following spinal anesthesia than in those with uncomplicated postanesthetic courses. It has also been shown that restoration of normal cerebrospinal fluid pressure by the injection of saline often relieves the symptoms.[14-17] The presence and persistence of the dural opening have been demonstrated in several ways. In myelography with special x-ray techniques, large quantities of fluid have been noted in the epidural space if ordinary lumbar puncture has been done within the previous two to four days.[13] Also, a needle tract in the lumbar meninges eleven days after the puncture and the presence of a dural fistula as long as fifteen days after the puncture have been demonstrated microscopically.[18, 19, 20]

If this theory is correct, it would seem that all patients in whom thecal puncture is performed should develop headache, but this is not true, and the reason it does not occur would undoubtedly give us the answer to the complete prevention of this situation. It has been proposed that because the arachnoid is loosely adherent to the dura it is usually swept against the persistent dural opening thus acting as a plug to prevent a continual leakage of fluid and a subsequent fall in cerebrospinal fluid pressure.[21] It is only when the defects in the two layers are superimposed that fluid loss occurs and the decreased pressure results.

Characteristics of the Headache.—The headache usually begins between the first and third postanesthetic days and its most characteristic feature is that it is initiated by assuming an erect position and promptly relieved by lying down. The location of the pain is variable, but it is most often noted in the occipital region and in the trapezius and neck muscles; nuchal rigidity, dizziness, and nausea may be present. The duration is also variable, but it usually has disappeared or is definitely improved by the fifth or sixth postpartum day. Most of the headaches attributable to spinal anesthesia are moderately severe and require analgesics for their control. Mild headaches are not uncommon after delivery without dural puncture, and certainly cannot be considered as due to spinal anesthesia; mild, transient headaches in patients who have had spinal anesthesia are not necessarily attributable to the anesthetic.

Materials and Methods

A total of 918 women to whom spinal anesthesia was administered for delivery in the Temple University Hospital are included in this study. Of these, 628 were private and 299 ward patients. The anesthetics were administered by a total of 18 physicians, 17 of whom were Residents on the Obstetric Service, who had followed the patients throughout their labors. In 690 cases the anesthetic agent was administered through 26 gauge needles and in

228 through 20 and 22 gauge needles. The technique for the administration of saddle block anesthesia varies little from that already reported. With the patient in the sitting position the back is prepared with ether and tincture of mercuric chloride and a 2 inch, 20 gauge introducer inserted usually at the interspace below the third lumbar vertebra, until firmly imbedded in the interspinous ligament. It is not necessary to penetrate this ligament or the ligamentum flavum completely; if the introducer is firmly imbedded in the ligament it will splint the smaller needle and further penetration with the latter can then be accomplished without difficulty. After the 20 gauge needle is properly placed, a 3 inch, 26 gauge needle is threaded through it and the dura is penetrated. Considerably more time is required for leakage of spinal fluid through this needle than through larger ones. Spinal fluid may be gently aspirated with a dry syringe to prove that the dura has been punctured. With the patient still in the sitting position a hyperbaric solution containing 5 mg. of Pontocaine increased to a total of 1 c.c. by the addition of 10 per cent dextrose is added. The maximum injection speed obtainable by the exertion of moderate force on the plunger of the syringe is necessary to obtain uniform anesthesia to the level of the ninth to tenth thoracic segment. It is almost impossible to inject too rapidly through the small needle, but low levels are common with an inadequate pressure and slow injection. The patient remains upright for 30 seconds following the injection and then is placed flat on the delivery table with her neck acutely flexed by a pillow under her head. Blood pressure, pulse, and fetal heart sounds are taken every minute for ten minutes, and the level of anesthesia is checked several times during this period. The blood pressure and pulse are taken and recorded at less frequent intervals throughout the delivery, and for one hour post partum.

With the 20 and 22 gauge needles a direct dural puncture was made and the solution was injected over a five-second period. The remainder of the technique was as described. In 69 instances (10 with 26 gauge and 59 with the 20 and 22 gauge needles) the injection was made with the patient in the lateral position, after which she was placed flat on her back with a pillow under her head for thirty seconds. At the end of this time the table was then elevated to a 15 degree angle which was maintained until the anesthetic agent was fixed.

Results

All patients were visited twice daily by the Resident staff and in an attempt to eliminate suggestion were questioned only about general complaints. Leading questions, particularly concerning headaches, were avoided, but each patient was encouraged to report any symptom no matter how trivial. If a complaint of headache was registered, complete details were then obtained and an attempt made to classify it as to cause and severity. It was not difficult to recognize the typical postspinal headache since it usually was moderately severe and different from the patient's usual headaches. A headache which did not vary from those frequently experienced was not attributed to the type of anesthesia and was labeled as atypical. Two-thirds of the atypical headaches were mild and transient.

Since the results and the complications associated with the use of the 20 and 22 gauge needles were comparable, they will be considered together. In 206, or 90 per cent of the patients, anesthesia adequate for delivery was obtained from the original blocks. The remaining 22 required some sort of supplemental anesthesia. A total of 56, or 24.1 per cent, of the patients complained of headache during the postpartum period, of which 39, or 17.1 per cent, were thought to be typical of those following spinal anesthesia. Of those,

20, or 51 per cent, were severe and the remainder mild to moderate. Headache was noted in 29 per cent of the private patients as compared to 17 per cent of the ward. In 228 cases there were 3 failures, or 1.3 per cent.

Of 628 patients in whom spinal anesthesia was attempted with the 26 gauge needle, in 30 the subarachnoid space was accidentally entered with a 20 gauge introducer, or there was failure to puncture the dura with the smaller needle. In 579 cases, or 92 per cent, the spinal anesthesia was adequate for delivery. Supplemental inhalation anesthesia was required in 49 cases. Of the 628 patients, 48 had headaches, or a total of 6.8 per cent. Only 24 of the 48, or 3.4 per cent, were considered as being typical and of these only 7, or 29 per cent, were severe. Headache occurred in 8.3 per cent of the private patients and 5.4 per cent of ward cases.

Summary

In certain instances spinal anesthesia has definite advantages over other methods for obstetric delivery, but the high incidence of postanesthetic headache has led many to abandon its use. Since no method of treatment has proved entirely satisfactory there have been many recent attempts to explain the mechanism and to reduce the incidence of this complication. Among these is the theory that leakage of fluid through the large dural defects produced by puncture with a large needle plays a significant part in the production of the headache. The suggestion that the incidence can be reduced by the use of smaller needles is supported by the results of this study. This study has shown that the number of headaches after spinal anesthesia administered with a 26 gauge needle was 69 per cent less than if the dural puncture was made with one of a standard size.

Other advantages were noted with the use of the smaller needle. A maximum injection speed of the anesthetic solution produced by firm pressure on the plunger of the syringe produced constant levels of anesthesia at the ninth to tenth thoracic segments, thus eliminating the need to time the injection accurately by the clock. High levels were rarely encountered; in fact a level too low to relieve the discomfort of uterine contractions was common with less than maximum injection pressure. The fact that more time and skill are required for administration by this method adds an additional safety factor since the anesthetic can be administered only to those patients in whom the procedure can be carried out deliberately and carefully, thus eliminating the hurried puncture and injection often utilized for patients whose labor is progressing rapidly and in whom the careless use of "routine" spinal anesthesia is not only dangerous but unnecessary.

Among the disadvantages is the need for the initial insertion of a 20 gauge introducer. Should the dura be punctured at this time the good effects of the small needle are nullified and the incidence of headache will increase. The number of failures to puncture the dura and the tendency to insert the needle entirely through the canal are both somewhat increased because the smaller needle may slip between the fibers of the dural sheath without the obvious sensation or snap which is present with the large needle. Despite the dis-

advantages, all of which will decrease with experience, this technique offers a worth-while refinement in obstetrical spinal anesthesia and should be utilized more frequently.

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FURTHER OBSERVATIONS UPON THE USE OF INTRAVENOUS PITOCIN IN OBSTETRICS*

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IT HAS been 58 years since Oliver and Schafer[1] first investigated the physiologic effects of their crude extracts made from the pituitary body. In the brilliance of their work with crude adrenal extracts, from which Adrenalin sprang into fame, they failed to note the virtues of the pituitary extract. It remained for Dale,[2] 11 years later, in 1906, to demonstrate for the first time the oxytocic action of the posterior pituitary gland. Another 22 years elapsed before posterior pituitary extract was separated into two fractions, the oxytocic and vasopressor principles, by Kamm and his co-workers.[3] Blair Bell[4] in 1909 was the first to report a clinical application in obstetrical practice. He reported excellent success in the management of three cases of postpartum hemorrhage. In this classical paper Bell stated prophetically, "I am inclined to think that in the future we shall rely on infundibular extract to produce contractions of the uterus in many serious complications and difficulties."

The basic science studies concerning actomyosin (the fibrous protein complex), adenosine triphosphate (ATP), and the newer concepts of intracellular electrolyte metabolism, are all adding to our more intelligent interpretation of the pharmacology of posterior pituitary extract. Szent-Gyorgi,[5] Reynolds,[6] Corner and Csapo[7] and other investigators have contributed much to our increased knowledge of uterine biochemistry and physiology. Undoubtedly, du Vigneaud's recent announcement that he has isolated a crystalline pure oxytocic factor will stimulate further basic and clinical studies.

In the past, many investigators reporting on the use of pituitary extract have failed to reach valid conclusions or have condemned the use of this agent. One cannot accept the statement that expedients to hasten labor inevitably carry in their wake injury and even death to mother and baby.[8] We must accept the mass of favorable evidence that is now being collected and reported. Louros and Coutifaris[9] of Athens recently informed us of their experience with "10,000 accelerated and painless labors." Approximately two-thirds of this group received pituitary extract. Their results indicate a lessened morbidity and mortality for both mother and infant. Other investigators[10-16] in somewhat smaller series have reported similar favorable results. With increasing experience and additional clinical observations, we

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have continued the evaluation of pituitary extract, and its relationship to maternal and infant morbidity and mortality.

Our present series of 646 cases has been added to the 576 cases previously reported.[10] Since the second series was evaluated according to the same criteria used in the first series, the total of 1,222 cases has been considered as one composite group. No cases were excluded from the clinical study. The patients were delivered upon the private and ward services of the Flower and Fifth Avenue Hospitals. This number of cases represents approximately 12 per cent of the patients delivered during this study.

Method

The method is essentially unchanged from that previously reported.[10] The product used throughout was Pitocin administered intravenously in a 1:1,000 dilution. We now advise an initial rate of flow of 4 to 10 drops per minute for the first half hour. The subsequent rate of flow is variable and should be individualized according to resultant contractions. All patients received Demerol, 0.1 Gm., and scopolamine, 0.4 mg., just prior to the start of the infusion. It was rarely necessary to repeat the sedation.

Material

Intravenous Pitocin was employed as an induction method in 672 cases (54.9 per cent) and to supplement labor in 550 cases (45.1 per cent).

The total induction group included 239 patients in whom a complication of pregnancy made termination desirable, and 433 cases in which induction was elective (Table I).

TABLE I. INDICATIONS FOR INDUCTION OF LABOR WITH INTRAVENOUS PITOCIN

Elective induction	433
Premature rupture of membranes	145
Toxemia	56
Antepartum fetal death	13
Abruptio placentae	10
Diabetes	3
Hydramnios	2
Miscellaneous	10
Total	672

The group that received Pitocin infusion as supplemental therapy included 173 patients with uterine inertia, 136 of whom had vertex presentations, 25 breech presentations and 12 twin pregnancies. In 341 cases, Pitocin infusion was used to supplement early labor and in 36 cases it was employed as a test of labor.

TABLE II. INDICATIONS FOR SUPPLEMENTAL THERAPY WITH INTRAVENOUS PITOCIN

Inertia	136
Inertia with breech	25
Inertia with twins	12
Early first stage of labor	341
Test of labor	36
Total	550

There was nearly equal distribution between patients pregnant for the first time and those with previous pregnancies. No patient received intravenous Pitocin who had more than four pregnancies (Table III).

TABLE III. PARITY OF PATIENTS WHO RECEIVED INTRAVENOUS PITOCIN

Para 0	625
Para i	439
Para ii	126
Para iii	27
Para iv	5

The ages of the patients ranged from 15 to 45 years, with 830 falling in the third decade of 20 to 29 years (Table IV).

TABLE IV. AGE RANGE OF PATIENTS WHO RECEIVED PITOCIN INFUSION

YEARS	NUMBER
15-19	34
20-24	360
25-29	470
30-34	253
35-39	98
40-45	7
Total	1,222

Results

In all successful cases, rhythmical intermittent uterine contractions resulted from as little as 25 to 50 c.c. of the Pitocin infusion within the first half hour of its use. These contractions cannot be distinguished clinically from spontaneously effective labor. Complete relaxation of the uterus was apparent between the contractions. The frequency and intensity of the uterine contractions can be controlled by the rate of flow. Prolonged contractions, seen primarily early in our experience, were readily controlled by discontinuance of the infusion. In those cases in which the infusion infiltrated or was discontinued, a decrease in the effectiveness and quality of the contractions was noted. It is believed that the continuous absorption, metabolism, and excretion afforded by the intravenous route serve to maintain an efficient therapeutic level.

Maternal Results.—

In the entire series of 1,222 there was no maternal mortality, no uterine rupture, and no untoward morbidity that could be attributed to the employment of this method.

Infant Results.—

There were 1,234 infants delivered of 1,222 mothers. There were 26 infant deaths (Table V). Sixteen of these were antepartum deaths which occurred prior to the use of the Pitocin infusion. Five were intrapartum and 5 were neonatal deaths.

The intrapartum deaths were caused in 2 cases by congenital atelectasis, in 1 case by prolapsed cord, and in one case the infant was born of a toxemic mother with abruption of the placenta at 25 weeks' gestation. There were but 5 neonatal deaths which were possibly related to the Pitocin infusion directly or indirectly. In 2 instances forceps applications failed, in a third case the mother had an associated severe toxemia, in a fourth case there was a coexistant abruptio placentae, and in the fifth case the infant perished soon after birth from cerebral anoxia associated with a tightly constricting cord around the neck (Table V).

The total of 26 fetal deaths represents an uncorrected gross mortality of 2.1 per cent and a corrected infant mortality, in cases where the fetal heart was heard at the onset of the infusion, of 0.4 per cent.

TABLE V. FETAL MORTALITY IN 1222 DELIVERIES OF 1,234 INFANTS FROM MOTHERS TREATED WITH INTRAVENOUS PITOCIN

Antepartum deaths (prior to the use of Pitocin)		16
Cause undetermined	7	
Toxemia	3	
Late missed abortion (6 months)	4	
Premature separation of placenta (23 weeks)	1	
Breech presentation	1	
Intrapartum deaths (stillborn)		5
Congenital atelectasis	2	
Placenta previa with premature infant	1	
Prolapsed cord at delivery	1	
Toxemia with premature separation of placenta at 25 weeks	1	
Neonatal deaths		5
Toxemia	1	
Abruption of placenta	1	
Cerebral anoxia (cord around neck)	1	
Failed forceps, cesarean section	2	
Total		26

Results According to Indication.—

In the 672 cases in which Pitocin infusion was used for the induction of labor, it was found successful in 641 instances (95.4 per cent) (Table VI).

TABLE VI. RESULTS OF INTRAVENOUS PITOCIN INFUSION ACCORDING TO GENERAL OBSTETRIC INDICATION

	TOTAL	NUMBER SUCCESSFUL	PER CENT SUCCESSFUL
Induction	672	641	95.4
Inertia	173	167	96.5
Early first stage	341	341	100
Test of labor	36	36	100
Total	1,222	1,185	96.9

In this entire study no case was considered successful unless an induction of true labor had been achieved upon the first attempt. In this series the failed cases included 31 women in the induction group and 6 cases in the inertia group. The highest failure rate of 6.6 per cent in the induction group may be compared to 21.0 per cent reported by Labate and Barbaro,[14] 26 per cent reported by Gordon,[12] and 9.0 per cent in Kaufman's[17] study.

Lubin[15] observed no failures in his inertia group. Hellman[18] reported 11.7 per cent failure in 401 cases of functional uterine dystocia. Labate and Barbaro[14] found an 11.0 per cent failure in their total series of 36 inertia cases and it is interesting to note that they found a 25 per cent failure rate in the para 0 inertia group. In this study there were but 6 failures, 3.5 per cent of 173 patients receiving supplementation for inertia. The explanations for the success in the use of Pitocin in 1,185 women from the total series of 1,222 cases (96.9 per cent) appear to be twofold: (1) solution concentration, and (2) strict observance of induction criteria. Lubin and associates[15] found that there was a less successful response when using a 1:10,000 dilution and a more successful result with a 1:5,000 dilution of the infusion. In all the cases in this study the standard dilution factor of 1:1,000 was maintained. Whatever the indication, success can be anticipated when the criteria of favorability are present. These were described by Hanley[19] and emphasized by Eastman[20] and bear reiteration: there must be present a soft cervix, 50 per cent cervical effacement, 1.0 to 2.0 cm. of dilatation, and a pelvis through which one can be reasonably assured that normal delivery is probable.

Status of Membranes.—

The membranes were not deliberately ruptured in our inductive procedure. It was felt that cases with intact membranes should not be compromised by the presence of artificial and prematurely ruptured membranes. In the second series of 646 cases an attempt was made to evaluate the status of the membranes. They had been ruptured spontaneously more than 12 hours in 67 instances, 12 hours or less in 125 cases, and during the administration of the infusion in 249 cases. In 6 cases it was impossible to determine the status of the membranes.

Rupture of the membranes is apparently not a factor in the initial success of this method. Once labor is stimulated by the use of intravenous Pitocin, however, rupture of the membranes will enhance the effectiveness.

Length of Labor.—

The average length of labor of those patients in whom intravenous Pitocin was used for supplementation was approximately 4.5 hours for the primigravid and 3.0 hours for multigravid patients. As was anticipated, in the patients who were subjected to elective or indicated induction, the length of labor was somewhat increased. It averaged 7.0 hours for the primigravidas and 4.0 hours for the multigravidas. In the breech cases the average length of labor was 3.5 hours following the onset of the Pitocin infusion.

The good results obtained when intravenous Pitocin was used for supplementation of labor are to be expected. The presence of early labor is fairly reliable evidence of the favorability of the cervix. The use of Pitocin infusion is of particular value in those cases of inertia or desultory labor which are so often associated with an increased incidence of infection, exhaustion, and operative obstetrics.

The employment of this technique permits the use of adequate sedation without lengthening the labor or decreasing the efficacy of uterine contractions. In addition there is some evidence that Demerol has a synergistic effect in relaxation and dilatation of the cervix. The patients also receive the benefits of intravenous fluids and glucose to combat dehydration and exhaustion.

Methods of Delivery.—

Spontaneous delivery was effected in 448 cases while low forceps were used prophylactically in 641 cases (Table VII). Thus, 1.089 cases, (89.1 per cent) were delivered by a nonoperative obstetric procedure.

TABLE VII. METHOD OF DELIVERY FOLLOWING THE USE OF INTRAVENOUS PITOCIN

TYPE OF DELIVERY	PRIMIGRAVIDA	MULTIGRAVIDA	TOTAL
Spontaneous	100	348	448
Low forceps	431	210	641
Midforceps	47	24	71
Assisted breech	9	11	20
Cesarean section	34	8	42
Total	621	601	1,222

There were 20 assisted breech deliveries and all the infants save one that died ante partum, were born alive. By actually shortening the notoriously long and ineffective labor characteristic of breech presentation, the use of Pitocin infusion probably contributes toward a decrease in fetal mortality and morbidity. Lubin[15] and Gordon[12] report similar results.

The remaining 113 patients (9.2 per cent) were delivered by operative methods. There were 71 midforceps applications (5.9 per cent) and 42 cesarean sections, a section rate of 3.4 per cent in this series of 1,222 cases.

Cesarean Section.—

Cesarean section was performed in 42 cases, 3.4 per cent (Table VIII).

TABLE VIII. INDICATIONS FOR CESAREAN SECTION FOLLOWING THE USE OF INTRAVENOUS PITOCIN INFUSION

Failure of induction		4
Lack of progress		10
Breech presentation	3	
Unsuspected large baby	7	
Test of labor		19
Other		9
Total		42

Of the 36 patients given a test of labor to evaluate borderline cephalopelvic disproportion, 17 were delivered vaginally while 19 were subjected to cesarean section. As Hunt[21] suggests, the best indication for cesarean section is a failed test of labor. The use of intravenous Pitocin results in better uterine contractions, precludes exhaustion, combats dehydration, and affords a more effective test of labor. Obviously, one would consider any absolute disproportion as a contraindication to the use of a Pitocin infusion.

Lack of progress in descent, despite success in dilation and apparent active labor after initiation of a Pitocin infusion, was the second largest factor indicating the choice of cesarean section. In 3 instances the breech presentation failed to exhibit a progressive descent in patients with prematurely ruptured membranes, while in 7 other cases larger babies than anticipated were delivered. Diabetes, pre-eclampsia unresponsive to controlled antepartum care, and prolapsed cord complicating the pregnancy dictated section in the remaining cases.

Vasopressor Effect.—

As mentioned previously, the use of Pitocin afforded a standardized product with a predominance of oxytocic factor and minimal pressor effect. There was no evidence of increased blood pressure in either the toxemic or nontoxemic patients. The absence of vasopressor effect when Pitocin is used has also been reported by McCormick.[16]

Summary and Conclusions

Twelve hundred twenty-two patients received Pitocin intravenously in a 1:1,000 dilution for induction or supplementation of labor. The procedure was successful in 1,185 cases (96.9 per cent). A high success rate is understandable in the supplementation group and can be anticipated for the induction group if the criteria of favorability are present. There were 26 fetal deaths with an uncorrected mortality of 2.1 per cent and a mortality for cases in which the fetal heartbeat was heard at the onset of the infusion of 0.4 per cent. There were no maternal deaths and no morbidity attributable to the use of this procedure. The incidence of operative obstetrics was low, with 1,089 patients delivering spontaneously or by low forceps. Midforceps were employed in 71 cases (5.9 per cent) and cesarean section in 42 cases (3.4 per cent).

Intravenous Pitocin may be employed for either induction or supplementation of labor and to insure an adequate test of labor. It is not con-

traindicated in twin pregnancies, breech presentations, or patients with elevated blood pressure. Grand multiparity and absolute disproportion are contraindications to the use of Pitocin.

The intravenous method of administration of a dilute Pitocin infusion is a safer, more physiologic and more effective method of using a valuable therapeutic adjunct.

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INTRAUTERINE AND NEONATAL PNEUMONIA

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INTRAUTERINE and neonatal pneumonias do not receive the attention they deserve. They account for approximately 10 per cent of all deaths in this age group. There have been numerous reports in the literature in the past forty years, yet this condition is still not widely recognized. Considerable work has been done on these pneumonias, but many problems remain, including the etiology.

Snyder and Rosenfeld[7, 8] have demonstrated that respirations begin prior to birth and that amniotic fluid passes in and out of the lungs. These respirations were first noted in animals. When carbon particles were placed in the amniotic sac of rabbits, widespread dissemination throughout the lung occurred in one minute. When the fetus was rendered apneic by an anesthetic given to the mother, no carbon was found in the lungs. Similarly, the injection of radiopaque material into the human amniotic sac showed rapid dissemination throughout the lungs, and also into the gastrointestinal tract of the fetus. This has been demonstrated to occur as early as the thirteenth week of gestation. Following animal experimentation, work on human beings established that respiratory movements of the fetus could be observed through the abdominal wall in women close to term. Motion picture studies show two types of movements: (a) Rapid rate, approximately sixty per minute with a shallow excursion. (b) Slower rate, approximately fifteen per minute with a deeper excursion.

The inhalation of amniotic fluid is considered by Snyder to be a normal intrauterine fetal function. Additional evidence of this is seen in the frequent finding of squamous epithelial cells, fatty vernix caseosa, lanugo hairs, and meconium in the bronchioles and alveoli of fetal lungs, even in cases where respirations were not established after birth.

The intrauterine pulmonary exchange of amniotic fluid together with the inhalation of material from the birth canal during and immediately after birth explains a method whereby bacteria can enter the fetal lungs. Aspiration of infected amniotic fluid is now accepted as the usual method of contamination. But this does not explain every case and a second suggested mechanism is hematogenous spread from the mother. In one case observed by us this latter mechanism was nicely demonstrated. A young mother at term was admitted to the hospital with advanced pneumococcal lobar pneumonia. Because the mother was critically ill and because labor had begun, the membranes were

ruptured and delivery was completed. Both the infant and the mother died a few minutes later. The infant did not have histological evidence of pneumonia but a pure culture of pneumococci was obtained from the lungs.

Gosselin[3] in 1937 demonstrated the rate at which bacteria enter the amniotic fluid after the rupture of the membranes. In a series of forty-five cases, he carried out repeated bacteriological examinations of fluid before and after rupture. In only one, a macerated infant, was the liquor contaminated prior to rupture. He found a second important factor to be the presence of active labor. In patients with ruptured membranes not in active labor, 60 per cent became infected in twenty-four hours. When active labor was present 100 per cent became infected in twenty-four hours. Table I is a summary of the findings reported by Gosselin.

TABLE I. RELATIONSHIP OF RUPTURED MEMBRANES TO INFECTION

A. Rupture of Membranes to Delivery.—			
0- 6 hours	10 cases	1 case infected	10%
6-10 hours	13 cases	4 cases infected	30%
10-24 hours	12 cases	6 cases infected	50%
24+ hours	10 cases	6 cases infected	60%
B. Duration of Labor with Ruptured Membranes.—			
0- 6 hours	21 cases	1 case infected	5%
6-10 hours	13 cases	7 cases infected	54%
10-24 hours	5 cases	3 cases infected	60%
24+ hours	6 cases	6 cases infected	100%

In all instances the bacteria found were those commonly present in the vagina.

The reported incidence of intrauterine pneumonia varies from 6 to 51 per cent of autopsied fetal deaths. These cases are recorded from 1910 to 1947 and involve seventeen different autopsy series varying from 32 to 954 cases.

Several important clinical observations have been made. The mother is commonly afebrile. Premature rupture of the membranes and prolonged labor are often present. The baby may die of pneumonia before or shortly after birth. The placenta and membranes may show an inflammatory reaction.

The gross pathology of pneumonia at this early age cannot be easily recognized, nor can it be differentiated from atelectasis and/or diffuse congestion. Lungs often float in water, and bronchial exudate is not a feature. Pleurisy and lung abscesses are seldom seen.

The diagnosis can be made only by microscopic studies. The majority of these pneumonias are said to differ from those seen in adults. The inflammatory process is usually diffuse and bilateral. The exudate consists of varying proportions of polymorphonuclear leukocytes and mononuclear cells. This is usually present only in alveoli without involvement of interstitial tissue. The alveoli may contain varying amounts of squamous cells from the fetal skin, vernix caseosa, lanugo hairs, and meconium. The significance of these findings is not clear. It may be that fetal asphyxia stimulates the fetus to stronger attempts at respiration.

Often seen is a "hyaline membrane." This was first described by Johnson.[4] It consists of a homogeneous eosinophilic staining material which lines alveolar ducts, alveolar sacs, and some of the alveoli. In this series of Johnson and Meyer[4] (97 cases) a well-defined hyaline membrane was the most conspicuous finding in 8 cases. Farber and Sweet[2] described and emphasized the formation of hyaline membrane from cornified squamous cells and fat drops. Warwick[9] in her series of 43 cases noted meconium in 70 per cent, and suggested that the inflammatory process may be due to the bile salts in the meconium.

Eight bacteriologic studies have been reported from 1914 to 1935.[7]

TABLE II. BACTERIOLOGIC STUDIES FROM 1914 TO 1935

DATE	AUTHOR	NO. CASES	GRAM STAIN	CULTURE	BACTERIA ABSENT	BACTERIA PRESENT
1914	Hess and Thaysen	18	18	5	3	15
1925	Johnson and Meyer	76	62	0	36	20
1928	Hook and Katz	36	36	0	16	20
1932	Szlavik	14	14	0	11	3
1934	Warwick	43	43	0	32	11
1939	Thaisz	5	0	2	0	2
1932	Muller	2	2	0	0	2
1935	Rosenthal	6	6	0	1	6

The bacteria reported were mainly found in the air passages rather than in the parenchyma of the lung. They were not seen in the lung capillaries.

The types of organisms in order of frequency recorded were: 1. Staphylococci. 2. Streptococci. 3. Gram-positive Bacilli. 4. Gram-negative Bacilli. 5. Gram-positive Diplococci. All these organisms are commonly found in the vagina.

Present Investigation On Intrauterine and Neonatal Pneumonias

Our study on intrauterine and neonatal pneumonias was carried out on 71 cases. These were autopsied in the Winnipeg General Hospital between January, 1940, and December, 1951. (Since this time an additional eighteen cases have been recorded.) The clinical case records were obtained from the Departments of Obstetrics and Gynecology.

During this period of time there were 20,700 newborn infants discharged from the hospital and 406 stillbirths and 396 neonatal deaths. Autopsies were performed on 598 of the total of 802 infants that died. The incidence of pneumonia was 11.7 per cent in those cases autopsied. This figure is somewhat higher than the incidence recorded by Potter and Adair[6] (6 per cent), D'Esopo and Marchetti[1] (7 per cent), and Labate[5] (8 per cent).

Evidence of Maternal Infection.—

Seventeen mothers exhibited fever before or during delivery. Of these, 7 had an elevated temperature before the onset of labor. One mother had pyelitis and another pyelonephritis, both conditions present before labor. In one case the mother's Wassermann reaction was 3 plus, and the baby showed many signs of congenital syphilis. Two mothers had vaginal discharge. One was greenish and watery, the other brownish.

In addition, 17 mothers developed fever in the first week post partum. In 2 of these patients, postpartum thrombophlebitis developed.

Complications of Pregnancy.—

There appeared to be more than the average number of complications of pregnancy. These are summarized in Table III.

TABLE III. COMPLICATIONS OF PREGNANCY

Artificial rupture of membranes	5
Manual dilatation of cervix	1
Antepartum bleeding:	
a. First and second trimesters	5
b. Third trimester	6
Polyhydramnios	1
Prolapse of cord	2
Multiple pregnancy:	
a. Twins	1
b. Triplets	1
Maternal heart disease	2
Hypertension	1
Pre-eclampsia and eclampsia	5

The Method of Delivery.—

There were 58 vertex presentations: left occipitoanterior 28; right occipitoanterior 20; right occipitoposterior 3; left occipitoposterior 6; and right occipitolateral 1 (transverse arrest).

There were also 4 breech presentations, 1 transverse lie, 4 cesarean sections, and in 4 cases the method of delivery was unknown.

TABLE IV. DURATION OF LABOR IN SEVENTY-ONE CASES OF PNEUMONIA

	NO. OF CASES	PER CENT
0-8 hours	23	32.4
8-16 hours	17	23.9
16-24 hours	6	8.4
24-32 hours	6	8.4
32-40 hours	5	7.0
40-48 hours	1	1.4
Over 48 hours	4	5.6
Cesarean section	4	5.6
Unknown	5	7.0

TABLE V. THE INTERVAL FROM RUPTURE OF MEMBRANES TO DELIVERY

	NO OF CASES	PER CENT
A. Pneumonia, 71 Cases.—		
Under 1 hour	21	30.0
1- 2 hours	5	7.0
2- 6 hours	7	9.8
6-12 hours	1	1.4
12-24 hours	5	7.0
24-48 hours	5	7.0
Over 48 hours	15	21.4
Cesarean section	4	5.6
Unknown	8	11.4
B. Control Series, 200 Random Cases.—		
Under 1 hour	125	62.5
1- 2 hours	14	7.0
2- 6 hours	24	12.0
6-12 hours	12	6.0
12-18 hours	12	6.0
18-24 hours	6	3.0
24-48 hours	5	2.5
Over 48 hours	2	1.0

In the case of the transverse lie, prolapse of the cord occurred and an internal version with breech extraction was performed. These figures do not suggest any deviation in presentation from the normal average.

The Duration of Labor.—

The duration of labor was over twenty-four hours in 16 cases. In four cases labor lasted over forty-eight hours.

The Interval From Rupture of the Membranes to Delivery.—

Table V summarizes the intervals in the pneumonia series and in a control series. The control series consisted of 200 consecutive infants that did not have pneumonia, from the records of the Maternity Pavilion, Winnipeg General Hospital. In the control series, 62.5 per cent of the cases showed the interval from rupture of the membranes to delivery to be under one hour. In the pneumonia group, 21 cases, or 30 per cent, were in this category. In 12.5 per cent of the control cases the interval was over twelve hours. In the pneumonia group, the interval in 35 per cent of the cases was over twelve hours.

The Fetus.—

There were 7 stillbirths, 4 cesarean sections, and one case of birth in an intact sac.

Eighteen babies showed either asphyxia pallida or livida. Resuscitation was necessary in 13 cases. Mouth-to-mouth respiration was performed in 9 cases. Mechanical resuscitation was used in 2 cases. An intratracheal tube was used in one case.

The gestation periods were as shown in Table VI.

TABLE VI. GESTATION PERIODS, 71 CASES

Under 28 weeks	10	
28 weeks	3	55%
29-36 weeks	26	
37-40 weeks	31	
Unknown	1	

Twenty-six babies had a temperature of over 98° F. at some time from birth to death. One had a temperature of up to 105° F. with chills.

Cyanosis was the commonest recorded sign and occurred in 35 cases. Blue spells were noted in 21 cases. Weak, shallow, or irregular respirations were present in 26 cases.

The duration of life is shown in Table VII.

TABLE VII. DURATION OF LIFE, 71 CASES

Stillborn	10
0-12 hours	13
12-24 hours	11
24-48 hours	13
48-72 hours	7
72-96 hours	2
4- 6 days	4
Over 6 days	11

Only 6 of the placentas were available for study. None of these showed evidence of inflammation of the membranes.

Autopsy Findings.—

Lung weights: A comparison with normal fetal lung weights as given by Potter and Adair shows that in this series there was an increase in the average weight of the lungs.

The control series consisted of 50 cases taken at random from the records. These were cases where no pulmonary pathology was present. The lung

weights were comparable with the normals given by Potter and Adair. The crown-to-rump and crown-to-heel measurements in the pneumonia series corresponded to the normal measurements given by these authors.

TABLE VIII. OTHER AUTOPSY FINDINGS OF SIGNIFICANCE

Intracranial hemorrhage due to tentorial tears	12
Congenital heart disease	3
Multiple gross congenital anomalies	3
Liver degeneration (toxic due to pneumonia?)	2
Septicemia	2
Multiple skin abscesses	1
Meningitis	1
Colitis	1
Syphilis	1
Cellulitis of buttock	1

Other Findings: The associated findings listed in Table VIII were present in 22 of the cases.

Gross Appearance of the Lungs in the Pneumonia Series: In this series the gross examination did not offer a conclusive diagnosis in most of the cases. The increase in the average weight of the lungs has been mentioned. Most of the changes described were bilateral and diffuse, but in several cases changes were unilateral or confined to one lobe. The lungs in 21 cases were described as being atelectatic. Diffuse pneumonic consolidation was suggested in 22 cases and patchy consolidation in 7 cases. One case showed multiple abscesses and in two other cases there was a gross purulent pleural exudate. "Diffuse," "dark red," and "congested" were terms used to describe the lungs in 24 cases. In 6 cases there were prominent subpleural petechial hemorrhages.

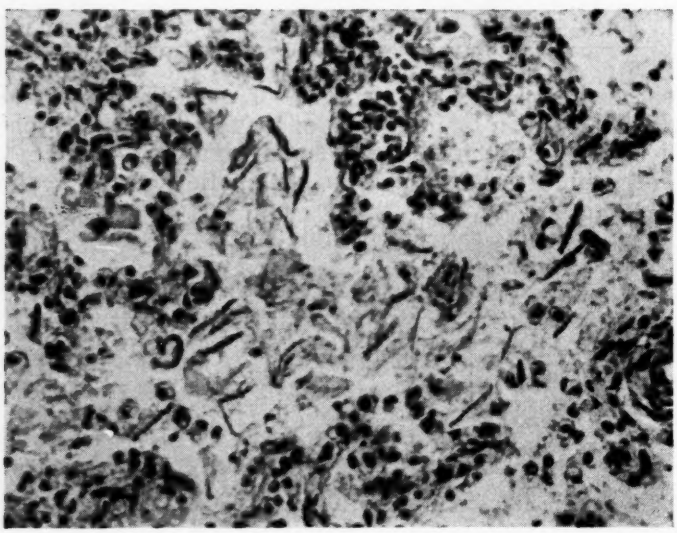

Fig. 1.—Intra-alveolar amniotic fluid contents. Material is mainly squamous epithelium. Although there is a minimal cellular reaction this is not pneumonia. (×300; reduced ⅛.)

Microscopic Criteria for the Diagnosis of Pneumonia

The histological diagnosis of pneumonia in the premature and term infant is much more difficult than in the adult. The unexpanded alveoli of the lung with cuboidal lining cells, numerous immature cells in the blood vessels, and the presence of amniotic fluid content are some of the features which may

cause confusion. The presence of a few intra-alveolar or intrabronchial leukocytes or monocytes probably does not constitute an early pneumonia. This is almost certainly a minimal response to the amniotic debris commonly present in these lungs. In this series, no case was called pneumonia unless the inflammatory reaction consisted of numerous intra-alveolar, intrabronchial, or interstitial inflammatory cells. Numerous microscopic fields had also to be involved. A number of cases were encountered during the survey, in which the lungs, alveoli, and bronchi were filled with numerous squamous epithelial cells and other amniotic-fluid debris. There was almost invariably a slight associated cellular reaction, which was mainly mononuclear. Only when there was a considerable number of mononuclear cells, associated with some polymorphonuclear leukocytes, was the condition in the lung called pneumonia (Fig. 1).

Fig. 2.

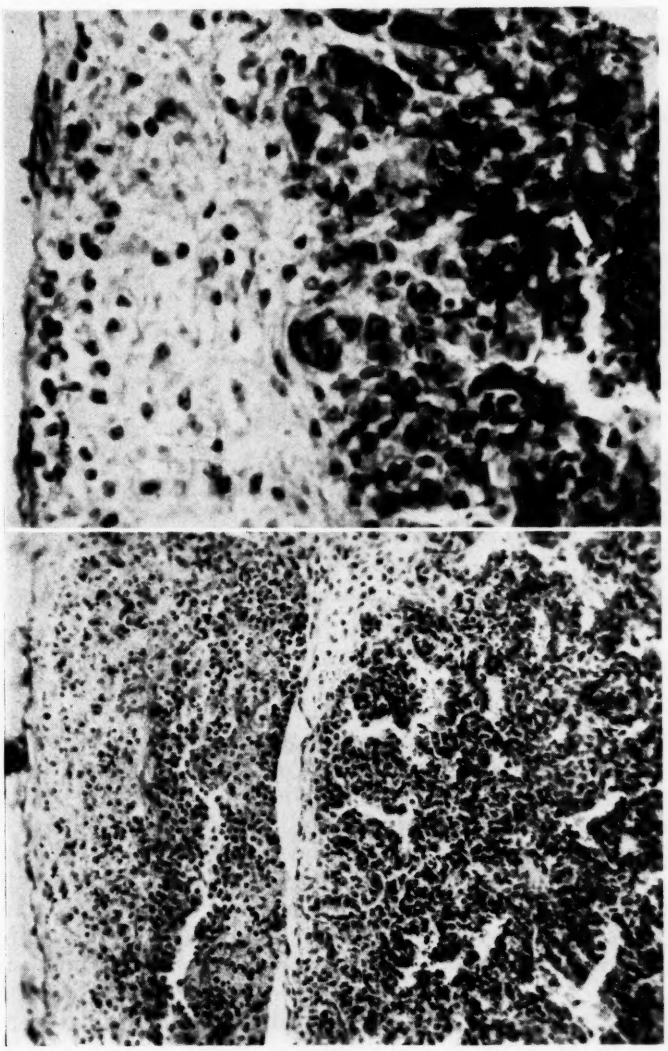

Fig. 3.

Fig. 2.—A-4767. Showing thickened and edematous pleura on left side infiltrated by mononuclear cells. (×400; reduced ⅛.)

Fig. 3.—Pleura on left. It is diffusely infiltrated by numerous polymorphonuclear leukocytes and covered by an acute exudate. (×150; reduced ⅛.)

Microscopic Pathology in Pneumonia

On the basis of the histological changes, the cases were divided into four groups. It is not suggested that these are actually different types of pneumonia or that they have a different etiology. The classification is done, however, to facilitate description, and also in an attempt to correlate infiltration patterns with bacteriology. Certain observations were made that were common to all the cases. In 95 per cent of the cases the pneumonias were bilateral, with a diffuse distribution of the infiltration.

A. Diffuse Acute Pneumonia.—

Forty-eight cases, or 67 per cent of the series, were of this histological type. The lungs in these cases are characterized by a diffuse, predominantly polymorphonuclear infiltration. There is complete absence of, or minimal, bronchial involvement.

Pleura: Most showed some thickening, edema, and slight cellular infiltration, the predominant cells being lymphocytes and monocytes. In only 2 cases was there an extensive acute cellular pleural reaction (Figs. 2 and 3).

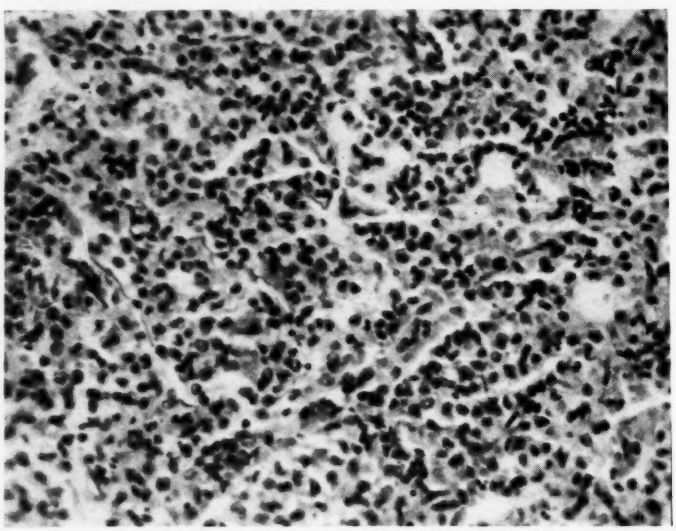

Fig. 4.—A-5964. Showing diffuse acute pneumonia. Alveoli contain numerous polymorphonuclear leukocytes with scattered epithelial cells and some granular debris. (×300; reduced ⅛.)

Bronchi, major and minor: These rarely contain a cellular exudate. The bronchial mucosa is congested but the epithelium is intact. The bronchial walls occasionally show a minor degree of inflammatory infiltration, when they are adjacent to areas of extensive alveolar infiltration. Most bronchi do not contain debris, squamous epithelium, or meconium.

Vessels: The vessels located in the involved areas occasionally show slight edema with separation of the cells of the adventitia and media together with a minimal inflammatory infiltration, usually mononuclear. Thrombi are not seen in this group. No obvious leukocytosis is present in the blood seen in the larger vessels.

Alveoli: The main pathology is the intra-alveolar and interstitial infiltration of the lung parenchyma by polymorphonuclear leukocytes (Fig. 4). These changes are bilateral and diffuse. Although the infiltration is diffuse, the intensity of infiltration varies from area to area. In this respect the distribution is different from that seen in classical adult lobar pneumonia. The infiltration almost invariably involves nonexpanded alveoli. The polymorphonuclear leuko-

cytic response in the lumina of the expanded alveoli is much less marked although often the walls show an intense interstitial reaction. The alveolar polymorphonuclear leukocytic infiltration is usually associated with a few lymphocytes and/or monocytes. Alveoli in 43 per cent of the cases contain some minimal amniotic fluid debris, usually squamous epithelium. In only 2 cases was there any considerable amount of amniotic fluid present. In those cases

Fig. 5.

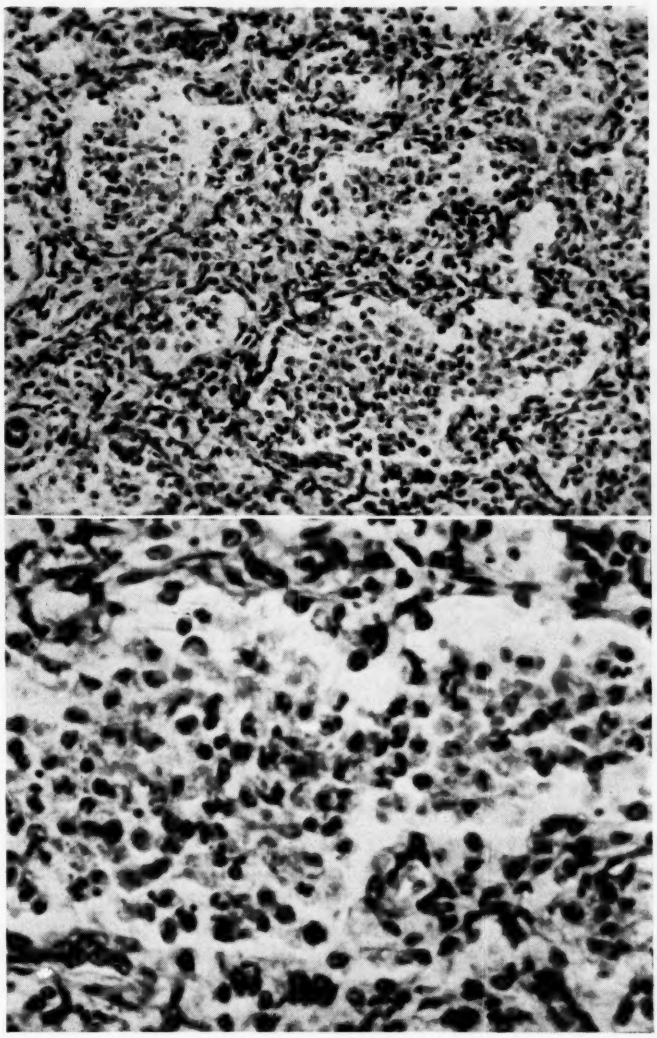

Fig. 6.

Fig. 5.—A-6021. Acute diffuse pneumonia. Alveoli are filled with polymorphonuclear leukocytes. Interstitial tissue is also infiltrated with similar cells. (×200; reduced ⅛.)

Fig. 6.—A-6021. Acute diffuse pneumonia. Same field as Fig. 5, showing details of leukocytes in the alveoli. (×450; reduced ⅛.)

with amniotic fluid content, there was no clear-cut relationship between the intensity of the inflammatory reaction and the amount of amniotic fluid present in the lungs. Areas of intense polymorphonuclear leukocytic infiltration are seen in the absence of amniotic fluid, as well as in association with it (Figs. 5 and 6). Similarly, some areas where amniotic debris is plentiful show no inflammatory

reaction. Albuminous fluid was present in a number of the cases, but in only one case was there any definite fibrin. The presence of granular pigment in the alveoli is difficult to evaluate.

Interstitial tissue: In most cases there is thickening of the alveolar walls with congestion, which in some cases is very marked. Rarely does the alveolar wall show necrosis even when associated with an intense inflammatory reaction. In most cases there is a fairly prominent infiltration of the alveolar wall by polymorphonuclear leukocytes. This appears to occur early, since it is often well marked in areas where there is minimal intra-alveolar leukocytic infiltration.

B. Diffuse Pneumonia, Histological Reaction Predominantly Mononuclear.—Eleven cases, or 15 per cent of this series, fall into this group. In these cases, the cellular infiltration was predominantly mononuclear with a diffuse distribution. In all cases there is an associated polymorphonuclear leukocytic infiltration, but these rarely exceed 25 per cent of the cells present (Fig. 7).

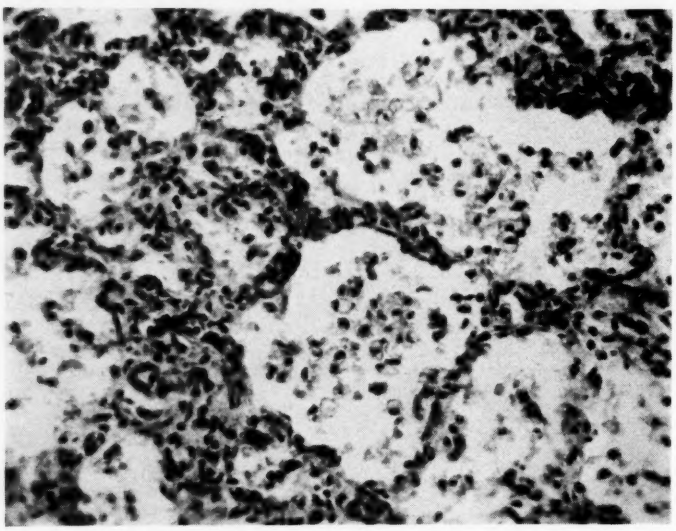

Fig. 7.—A-5847. Diffuse mononuclear type of pneumonia. Alveoli contain numerous mononuclear cells with a few polymorphonuclear leukocytes. (×250; reduced ⅛.)

Many of the mononuclear cells are large and of the phagocytic type having abundant vacuolated cytoplasm. This reaction is the type seen in so-called "aspiration pneumonia." All of these cases show minimal amnoitic fluid, chiefly in the alveoli. In no case was the amount of amniotic fluid in the lungs even moderately marked. The pleura of most cases show minimal edema and chronic round-cell infiltration. One case in this group is worthy of special mention.

CASE NO. 7515.—This was a premature infant of 36 weeks' gestation delivered by cesarean section, weight 1,690 grams at birth. The infant ran a swinging temperature, up to 103° F., from the third day until death on the ninth day. On the sixth day, a cellulitis of the buttock with scrotal edema and necrosis developed. The infant was treated with intramuscular penicillin. Autopsy findings include the previously mentioned cellulitis together with a diffuse, intense, predominantly mononuclear, intra-alveolar and intrabronchial infiltration. Many small and medium-sized arteries showed an intense necrotizing panarteritis and periarteritis. The lumina of these vessels were filled with thrombi; the walls were diffusely infiltrated with numerous eosinophils and polymorphonuclear leukocytes. *Bacillus pyocyaneus (Pseudomonas aeruginosa)* was cultured from the lung and from the abscess on the buttock. No other visceral changes were noted and vessels of the other organs did not show arteritis (Fig. 8).

C. Pneumonia, Bronchial and Peribronchial in Type.—

Four cases, or 5 per cent, were bronchopneumonia. The lumina of the major and minor bronchi and bronchioles were filled with polymorphonuclear leukocytes. The alveoli surrounding these bronchi showed a patchy intra-alveolar polymorphonuclear infiltration. The walls of the bronchi were congested, the mucosa was intact. The interstitial tissue was infiltrated with varying numbers of acute and subacute inflammatory cells. A few blood vessels in the involved area showed a minimal cellular infiltration, usually adventitial. Aspirated intra-alveolar amniotic fluid debris was not a feature in these cases. The pleura showed a minimal cellular reaction (Figs. 9 and 10).

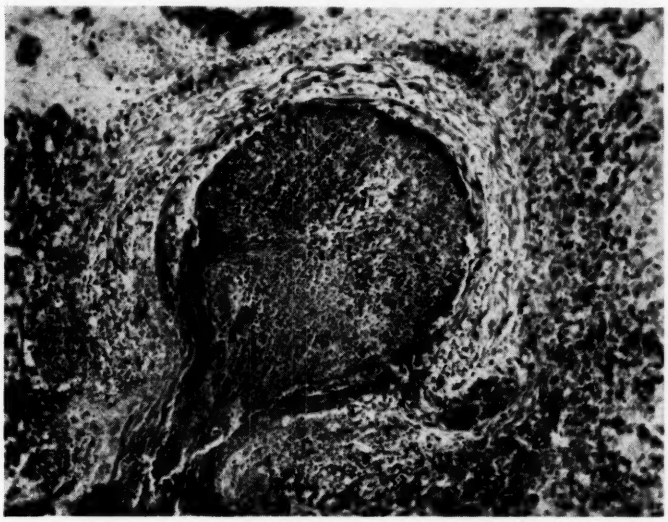

Fig. 8.—A-7515. Medium-sized artery showing an acute polyarteritis. The lumen contains a thrombus. (×125; reduced ⅛.)

D. Pneumonia Associated With Hyaline Membrane.—

Eight cases, 11 per cent, of this series of cases of pneumonia were associated with a fairly prominent hyaline membrane. The inflammatory reaction was predominantly polymorphonuclear. In a few cases, however, there was an associated mononuclear infiltration. In one case the cellular response was entirely mononuclear. Most of these were acute diffuse pneumonia of the Group A type. The hyaline membrane present varied, but was usually diffuse. It lined the alveolar ducts and presented an amorphous, eosinophilic appearance. There was no relationship between the intensity of the inflammatory reaction and the presence of the hyaline membrane. No case of hyaline membrane (resorption atelectasis) was included in this series unless associated with a pneumonic inflammatory reaction (Fig. 11).

In only 2 of the 71 cases in this series was there evidence of a generalized infection (septicemia). In the other cases microscopic evidence of infection was confined to the lungs and pleura.

Significance of Amniotic Fluid Contents

As shown in Table IX, in most of the cases there was some amniotic fluid debris present in the lungs. The constituents of amniotic fluid which can be identified are albuminous fluid, fat from the vernix caseosa, lanugo, cornified epithelial cells, and bile salts from meconium. It is said that the latter can be recognized as small masses of various sizes and shapes, composed of brown granules.

The lungs in many cases of intrauterine and neonatal death, apart from the series described, were reviewed. The finding of amniotic fluid contents was the rule, regardless of the cause of death. As the survival time increases, the amount of amniotic fluid contents decreases. Many nonpneumonia cases show marked amniotic fluid contents in the lungs and cellular reaction is absent. The cornified epithelium is the easiest to recognize histologically, and

Fig. 9.

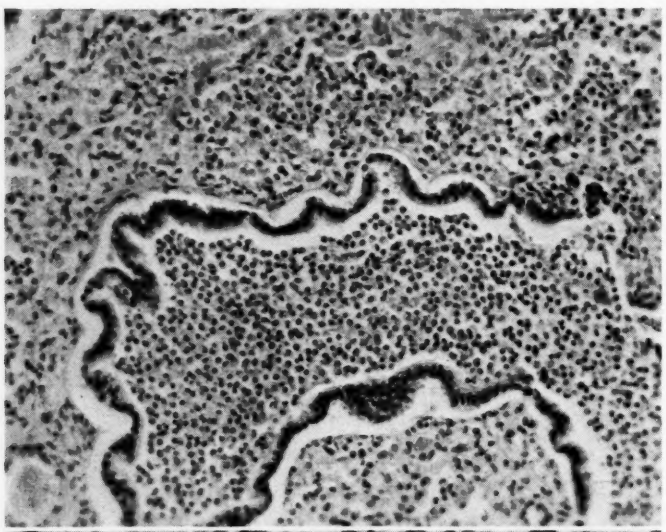

Fig. 10.

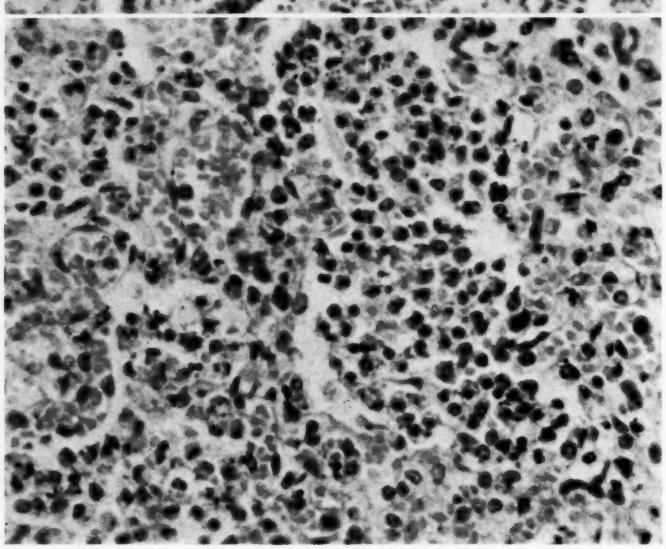

Fig. 9.—A-6817. Bronchopneumonia. Bronchus is filled with polymorphonuclear leukocytes and a few squamous epithelial cells. (×150; reduced ⅛.)

Fig. 10.—A-6817. Same case as Fig. 9. Higher magnification showing details of infiltration in the alveoli. (×250; reduced ⅛.)

bile pigment the most difficult. In many routine formalin-fixed paraffin sections much brown granular pigment is found. This pigment gives a negative Prussian-blue staining reaction. Treating the slides with picric acid and alcohol to remove the formalin-precipitated pigment results in complete removal of all the pigment. It is now proposed to use histochemical methods for defi-

nite identification of the pigment granules found in the lung. Until this has been done no definite conclusion can be reached. Meconium, however, does not appear to be present as frequently as stated by numerous other authors. Since few authors state their criteria for identification of meconium pigment, their reported results are difficult to evaluate.

An attempt was made to assess the relationship of amniotic fluid content to the inflammatory reaction. The amount of amniotic fluid content was graded as follows: present +, slight to moderate amount ++, and fairly marked to marked +++. The inflammatory reaction was similarly graded. Although occasionally the grading of both is similar, in the majority of cases they are dissimilar. As emphasized in the discussion of histological changes, there does not appear to be any constant relationship between the amniotic fluid contents and the inflammatory reaction.

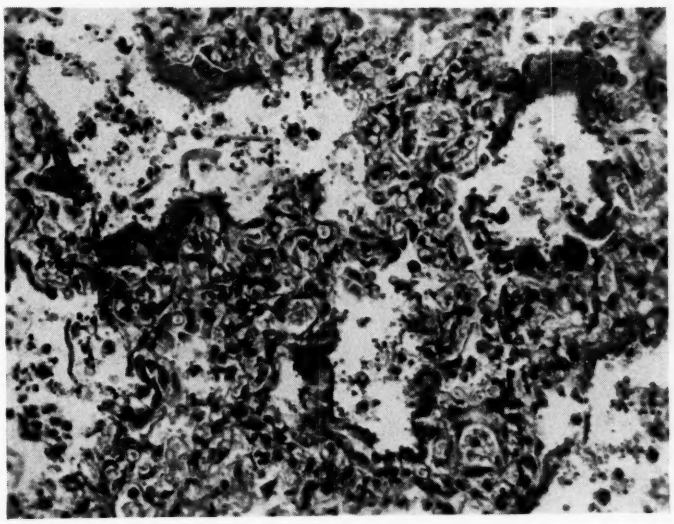

Fig. 11.—A-6198. Note amorphous hyaline membrane lining alveolar ducts. Lumen contains some amniotic debris. In other areas there is an intense polymorphonuclear leukocytic and mononuclear reaction. (×150; reduced ⅛.)

Bacteriology

When this investigation was begun, lung cultures were not taken routinely. This procedure was established with the use of the following technique at autopsy. The lungs are removed from the chest cavity, and a heated electric soldering iron is used to sterilize by searing the pleural surface over a 2 cm. area. This produces a friable, coagulated area to a depth of approximately 1 to 2 mm. A sterile swab consisting of a small amount of cotton on the end of a wooden applicator is introduced into the lung parenchyma through this seared area. These swabs are then cultured on both aerobic and anaerobic media.

In spite of the fact that this was established as a routine procedure, in only 36 cases, or 50 per cent of the series, were cultures obtained. Of these 36 cultures taken, 34, or 92 per cent, were positive. Tissue Gram's stains were done in all the cases using the paraffin blocks of the lung sections. Gram's stains were also done on sections of the other viscera to exclude gross contamination of the entire fetus.

The results of the postmortem lung cultures and smears together with the Gram's stains of the paraffin section of lungs are listed in Table IX.

TABLE IX. SUMMARY OF SEVENTY-ONE CASES

AUTOPSY NUMBER	SURVIVAL TIME (HOURS)	RUPTURE OF MEMBRANES TO BIRTH		GESTATION PERIOD (WEEKS)	DEGREE OF CELLULAR INFILTRATION	R.B.C. INFILTRATION	AMNIOTIC FLUID	TIME OF DEATH TO AUTOPSY (HOURS)	POSTMORTEM CULTURES OF LUNGS	P.M. SMEARS OF LUNGS	TISSUE GRAM'S STAINS, LUNGS
		HOURS	MINUTES								
Diffuse Pneumonia, Cellular Reaction Predominantly Polymorphonuclear.—											
*5882	17	39 Artificial rupture	0	35	++	+	+	82	None	None	Negative
5930	41	11	45	40	++		++	24	None	None	Gram-pos. diplococci
5972	22 days	Cesarean		40	+		+	9	*B. coli*	None	Gram-pos. diplococci Gram-pos. streptococci
*5973	15	4	43	39	+++		+++	24	Throat of intern giving mouth-to-mouth, hem. strep. and Staph.	Same as culture	Streptococci Staphylococci
6021	65			25	+ (patchy)		0	84	None	None	Gram-pos. diplococci
6178	18 days	0	15	30	++		+	80	None	None	Gram-pos. streptococci
6190	13 days	133	0	24	+++		0	55	None	None	Negative
6292	22	0	15	28	+		+	60	None	None	Gram-pos. diplococci
6294	1	1	57	28	+++	+++	0	48	None	None	Negative
6400	Stillbirth	4	31	36	++		+	48	*B. pyocyaneus*, hem. *Staph. aureus*, coag. pos.	Pus and gram-pos. cocci	Negative
6516	96	1	35	31	+++		0	28	*B. coli* *Strep. fecalis*	None	Gram-pos. cocci

6548	28	20	0	33	+++		+	48	Anaerobic strep.	None	Negative
6605	40	0	37	40	++		+	36	*Staph. aureus*	Negative	Negative
6645	15	?		32?	++		0	36	Staphylococci	None	Gram-pos. cocci (Staph.)
6711	7.5	?		33	++		++	12	*Streptococcus viridans*	None	Negative
6817	11 days	7?	0	30	++		++	48	*Streptococcus viridans*	None	Gram-pos. cocci
7059	44	0	17	40	++	+++	+++	15	None	None	Gram-pos. diplococci and streptococci
7069	32	26	30	38	++	++	+	24	Staphylococcus, coag. pos.	None	Negative
7116	21	34	0	37	+++		+	48	Negative	None	Negative
7395	9	?		31	+		0	48	None	None	Negative
7448	18 days	?		40	+		0		Hem. *B. coli*, *Strep. fecalis*	None	Gram-pos. chained cocci
46/4170	Stillbirth	?		20	++		0	6	None	None	Negative
47/2593	1 min.	0	1	27	+++		+	2	None	None	Negative
3659	120	0	30	30	+++		+	12 days	None	None	Gram-pos. cocci in chains
4304	144	0	1	32	++	+++	+	8 days	None	None	Negative
4767	120	15 Prolapsed cord, cesarean	11	33	++	+++	+	48	None	None	Negative
5083	71	0	9	41	++		+	24	None	None	Negative
5126	72	0	48	40	+++		+	24	None	None	Gram-pos. diplococci

TABLE IX. SUMMARY OF SEVENTY-ONE CASES—CONT'D

AUTOPSY NUMBER	SURVIVAL TIME (HOURS)	RUPTURE OF MEMBRANES TO BIRTH		GESTATION PERIOD (WEEKS)	DEGREE OF CELLULAR INFILTRATION	R.B.C. INFILTRATION	AMNIOTIC FLUID	TIME OF DEATH TO AUTOPSY (HOURS)	POSTMORTEM CULTURES OF LUNGS	P.M. SMEARS OF LUNGS	TISSUE GRAM'S STAINS, LUNGS
		HOURS	MINUTES								
5164	122	0	29	28	++		+	36	Pleura, hem. *Staph. aureus* Bronchi, hem. streptococcus	Streptococci	Negative
*5224	22 min.	114	0	38	+++		+	36	None	None	Negative
*5487	59	1? Born in taxi	0	40	+++		+	24	None	None	Gram-pos. cocci and diplococci
*5659	10	33	0	40	++	++	0	18	None	None	Gram-pos. streptococci and diplococci
5664	57	61	22	30	++	+++	+	15	None	None	Negative
8043	Stillbirth	132	0	40	+++	+	++	9	Hem. *Staph. aureus*, coag. neg. Mother on antibiotics during labor	None	Negative
6548	17	20	0	33	+++	+	0	48	Anaerobic strep.	Negative	Negative
8030	Stillbirth	66	0	40	+	++	++	9	*B. coli* *Staph. aureus*, coag. neg.	None	Negative
7677	11 days	0	3	41	++++ (Abscess)	++	0	6	*Strep. faecalis* *Staph. aureus*, coag. pos. (on antibiotics)	Negative	Small gram-neg. bacilli. Hem. influenzae?
7661	48	4?		41	+++	++	+	14	Hem. *B. coli*, *B. proteus*		Gram-neg. coliform bacilli

*6812	14 days	0	0	22	++		0	24	*B. coli, Strep. faecalis*	None	Gram-pos. cocci and bacilli
*6370	60	1	20	27	++	+++	0	50	*B. aerogenes, Strep. faecalis*	Gram-pos. diplococci	Gram-pos. cocci and diplococci, chain strep.?
5720	Stillbirth	12 days		40	+++	+	+	16	None		Negative
*4032	28	3	0	41	+++	++	++	55	None		Gram-pos. cocci and streptococci, coliform bacilli
7908	3.5	3	0	41	+++	+++	++	20	*B. coli, B. alkaligenes*	Negative	Negative
7817	15	0	7	41	++	+++	0	18	Negative		Negative
7800	7.5	20?	0	31	+++	++	0	22	On antibiotics. Hem. *Staph. aureus*, coag. neg.		Negative
7725	Stillbirth	75	0	41	+++	++	+	24	Anaerobic strep.		Gram-pos. cocci
7683	22	0	3	37	+++	++	+	24	B. hem. strep. *Staph. aureus*, coag. pos. *Strep. faecalis*		Negative
8178	Stillbirth	40 days	?	32?	++	++	0	100	*Staph. aureus*	None	Negative
Diffuse Pneumonia, Cellular Reaction Predominantly Mononuclear.—											
*6323	1.5	1	45	40	+	+++	+	36	None	None	Negative
6592	16	1	0	42	+		+	24	*Staph. aureus, Strep. viridans, B. coli*	Gram-pos. cocci	Negative
7515	9 days	Cesarean		36	+	+++	+	24	Lung, *B. pyocyaneus* Abscess of buttock, *B. pyocyaneus*	None	Gram-pos. cocci

TABLE IX. SUMMARY OF SEVENTY-ONE CASES—CONT'D

AUTOPSY NUMBER	SURVIVAL TIME (HOURS)	RUPTURE OF MEMBRANES TO BIRTH		GESTATION PERIOD (WEEKS)	DEGREE OF CELLULAR INFILTRATION	R.B.C. INFILTRATION	AMNIOTIC FLUID	TIME OF DEATH TO AUTOPSY (HOURS)	POSTMORTEM CULTURES OF LUNGS	P.M. SMEARS OF LUNGS	TISSUE GRAM'S STAINS, LUNGS
		HOURS	MINUTES								
5046	33	81	0	36	++		+	?	None	None	Negative
5568	7 days	2	0	40	+		+	7 days	None	None	Negative
5563	59	18	0	36	+		+	24	None	None	Negative
5606	36	0	34	32	+	+++	+	24	None	None	Gram-pos. streptococci and diplococci
5847	29	89	9	34	++	++	+	72	None	None	Gram-pos. streptococci
8333	22	0	18	39	++	+++	+	10	*B. aerogenes, B. pyocyaneus*	None	Negative
6183	Stillbirth	48	0	41	++	++	++	36	None	None	Negative
8220	Stillbirth	72	0	37	++	++	+		Hem. *Staph. aureus,* coag. pos.	None	Gram-pos. cocci, staphylococci
Bronchopneumonia, Cellular Reaction Predominantly Polymorphonuclear.—											
*5964	41	1	8	41	++		++	24	None	None	Negative
4882	7 days	0	5	35	+++	+++	+	48	None (Wassermann reaction +++)	None	Negative
7647	12 days	?		26	++		0	44	Skin infection, *Staph. aureus,* coag. pos.		Gram-pos. strep.
7905	48	10	0	41	++	+++	+	26	On antibiotics, *Staph. aureus,* coag. neg. *Strep. faecalis*		Negative

AUTOPSY NUMBER	SURVIVAL TIME (HOURS)	RUPTURE OF MEMBRANES TO BIRTH		GESTATION PERIOD (WEEKS)	TYPE OF INFILTRATION	DEGREE OF CELLULAR INFILTRATION	R. B. C. INFILTRATION	AMNIOTIC FLUID	TIME OF DEATH TO AUTOPSY (HOURS)	POSTMORTEM CULTURES OF LUNGS	P.M. SMEARS OF LUNGS	TISSUE GRAM'S STAINS, LUNGS
		HOURS	MINUTES									
Pneumonia Associated With Hyaline Membrane.—												
6198	26	40		36	Mono. P. M. N.	+		+	24	Hem. *Staph. aureus*, pneumococcus	None	Negative
6929	11	0	2	26	Mono. P. M. N.	++		++	60	Hem. *Staph. aureus*, hem. *Strep. faecalis*, *B. aerogenes*	None	Gram-pos. cocci
3752	8	0	2	32	P. M. N.	+++	+++	++	48	None	None	Negative
4814	6	Cesarean		33	Mono.	++		+++		None	None	Negative
5181	73	24	0	34	P. M. N.	+++	++	+++	13 days	None	None	Gram-pos. diplococci, gram-pos. cocci. Staph. (and pneumococcus?)
8029	36	0	10	31	P. M. N. Mono.	+	+++	++		Beta hem. strep.	Gram-pos. cocci	Gram-pos. cocci, staph.
7988	22	*		20	P. M. N.	+++	0	++	20	Pneumococcus	None	Negative
7984	8	32 Ruptured artificially	0	25	P. M. N. Mono.	+	+	++	2.5	Hem. *Staph. aureus*, coag. pos. *B. alkaligenes*. Mother on penicillin	Negative	Negative

*Mouth-to-mouth resuscitation used.

TABLE X. SUMMARY OF ORGANISMS RECOVERED FROM THE LUNGS BY CULTURE

	NO. OF CASES
Hemolytic *Staphylococcus aureus*, coagulase positive (*Micrococcus pyogenes*)	18
B. coli (E. coli)	8
Streptococcus faecalis	8
Hemolytic streptococcus	4
B. pyocyaneus (Pseudomonas aeruginosa)	3
Streptococcus viridans	3
B. aerogenes	3
Anaerobic Streptococci	2
B. alkaligenes	2
Pneumococcus	2
B. proteus	1
Hemophilus influenzae	1

The source of the organisms listed is speculative. Bacteria such as the pneumococcus and the influenzae bacillus are not normally found in the maternal vagina. In one case throat cultures were taken from the physician who had used mouth-to-mouth resuscitation. The throat pathogens were the same as those recovered from the infant's lungs.

Examination of tissue sections stained by Gram's method revealed organisms in the lungs in 29 cases. In 26 of these, the organisms were gram-positive streptococci, staphylococci, and diplococci; one showed gram-positive cocci and coliform organisms, one coliform organism only, and the other gram-negative bacilli which are morphologically *Hemophilus influenzae*. The distribution of these organisms was not constant. They were present with equal frequency in bronchi and alveoli and occasionally in lymphatics and capillaries. In Group A, all cases which had received mouth-to-mouth insufflation showed bacteria in lung sections. There was no relationship between intensity or type of histological reaction and the bacteria found in cultures or sections (Figs. 12 and 13).

Generally speaking, the bacteria present in inflamed tissue are probably the causative organisms. There are, of course, many exceptions to this statement. Cultures taken at autopsy are difficult to evaluate. Negative findings do not rule out the presence of bacteria during life, nor does a positive culture prove causation of the inflammatory disease.

Multiple factors enter into the evaluation of postmortem cultures. An attempt was made to assess critically our bacteriological findings as causative factors in the intrauterine and neonatal pneumonias.

Control Series

As a control series for the pneumonia cases with positive cultures, a group of 36 consecutive fetuses and infants without pneumonia, autopsied during the same period of time, were used.

Forty per cent of the cultures from the controls were positive, compared with the 92 per cent found positive in the pneumonia cases. The types of organisms found in the two groups showed no significant differences.

In an attempt to establish what factors might be important in obtaining positive cultures, the following information was tabulated in both pneumonia and control series: gestation period; administration of antibiotics to mother or infant; interval from rupture of membranes to delivery; use of resuscitation procedures; time of survival of infant; interval from death to autopsy; intensity of inflammatory reaction. From these, three main factors associated with positive cultures in the controls emerge. These are maceration, a long interval between rupture of membranes and delivery, and a long delay of the

autopsy. The common denominator of these factors appears to be an increased opportunity for contamination, and a long interval for bacterial growth. This explanation, however, does not suffice for all of the positive cultures in the controls.

A similar set of controls, for evaluation of organisms found in the tissues by Gram's stain, was used. In a series of nonpneumonic lungs, with negative postmortem lung cultures, bacteria were found in the tissue sections in 20 per cent of the lungs.

Fig. 12.

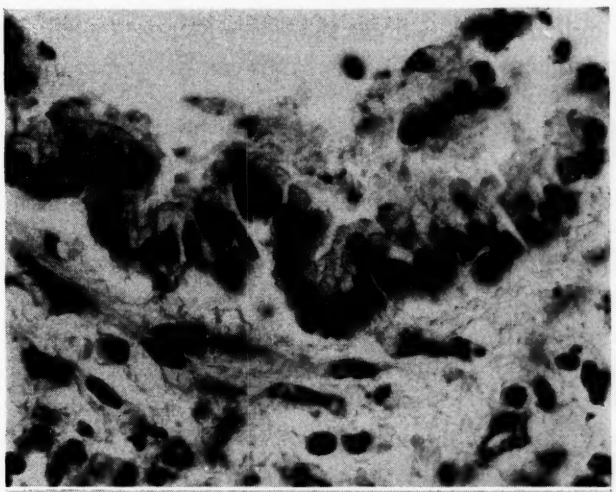

Fig. 13.

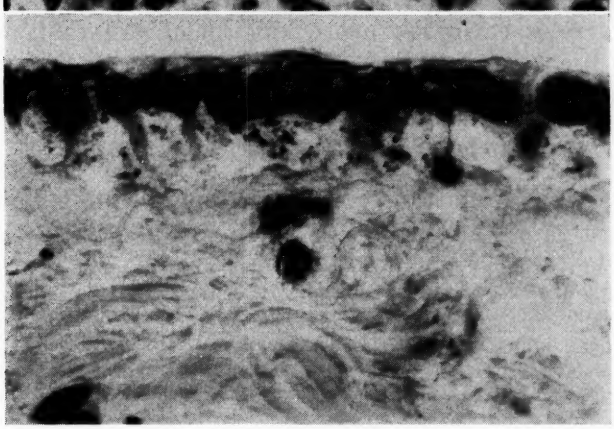

Fig. 12.—A-4032. Showing a small group of bacteria in the lumen of a bronchus. (×750; reduced ⅛.)

Fig. 13.—A-4032. Showing bacteria in the bronchial wall just deep to the intact surface epithelium. (×100; reduced ⅛.)

The study of these controls indicates that autopsy cultures as done in this series cannot be entirely accepted as proof of bacteriological cause of pneumonia, since 40 per cent of nonpneumonic cases had positive cultures. Only 20 per cent of these "false positive" cases had bacteria in paraffin sections of the lungs. Finding of bacteria in the tissue section is therefore significant. Bacteriological study is most reliable and significant when similar bacteria are found by culture and in the tissue sections.

Summary

A brief review of the literature on intrauterine and neonatal pneumonias has been presented.

Seventy-one new cases are summarized. These constituted 11 per cent of all intrauterine and neonatal deaths at the Winnipeg General Hospital.

In most cases positive cultures were obtained or bacteria were found in the tissue section of the lungs.

The control series also had a relatively high incidence of positive cultures, but bacteria were seldom found in the tissue sections of the lungs. Interpretation of bacteriological findings must therefore be made with caution.

Most pneumonias are of a diffuse, bilateral, predominantly polymorphonuclear leukocytic type.

Amniotic fluid content in the lungs does not appear to be a very significant etiological factor.

The highest incidence of pneumonia occurs in premature infants with early rupture of the membranes.

Recognition of the following facts might reduce the incidence of intrauterine pneumonia:

A. Since vaginal examination prior to delivery may infect both the mother and infant this should be done only when strictly indicated and then under the best aseptic technique.

B. Artificial rupture of the membranes should be restricted to cases where there is an absolute indication.

C. When there is early rupture of the membranes antibiotics should be given to the mother.

D. Mouth-to-mouth resuscitation is a hazardous procedure.

Conclusion

Seventy-one cases of intrauterine and neonatal death due to pneumonia have been investigated. Intrauterine pneumonia constitutes an important cause of death, and deserves wider recognition and study.

We wish to thank the following for their help in this investigation: Dr. Margaret Ledingham for initial assistance with the records, Dr. J. C. Wilt for help in bacteriology, Miss L. Nason for the photomicrographs, and Miss M. Melville for the special technical preparations.

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PUERPERAL TETANUS

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TETANUS is a dreaded and extremely deadly disease. In spite of modern, intensive therapy the mortality rate remains between 75 and 100 per cent. Puerperal tetanus is not only the most dangerous of all puerperal infections but is probably the most dangerous of all tetanus infections as well. DeLee has pointed out that the incubation period, being from four to twenty-one days, is considerably shorter than that for tetanus infections in general. It is interesting that in the fatal cases that have been reported the patients have died almost consistently between the tenth and twelfth postpartum days. The postpartum uterus forms a good culture medium for the anaerobic organism, *Clostridium tetani,* and absorptive conditions are excellent.

Puerperal tetanus is generally considered to be one of the rarest of puerperal infections and has attracted only a minor academic interest. Of the tetanus infections that gain entrance through the uterus, those following abortions are much more commonly seen than those following normal full-term deliveries. They are usually preceded by attempts at criminal interference by unsterile instrumentation or unsterile vaginal examinations at the time of delivery.

A total of 210 cases of postabortal tetanus and 114 cases of postpartum tetanus have been reported. Most cases have been reported from Europe with a few reports within the past twelve years appearing from England and the United States. Vinay in 1894 found the mortality rate in 106 cases to be 88.7 per cent. In 1898 Sepet[12] collected 125 cases, 48 of which were postabortal and 77 postpartum. The mortality rate in this series was 86 per cent. Schneider in 1926 reported 109 cases with a mortality rate of 91 per cent. Milnor[10] in 1928 reported that tetanus was prevalent in Hawaii, with a mortality rate of approximately 92 per cent. He reported a case of postpartum tetanus in which the mother died on the ninth postpartum day and the infant died of tetanus three days later, having been infected through the umbilical stump. Le Doze is quoted as having collected, in 1936, 19 cases from the French literature, 14 of which followed abortions. Maclean and Challen,[8] in 1941, reported one case of postpartum tetanus with recovery and stated that they were unable to find another case in the British literature at that time.

Weinstein and Beacham[15] in 1941 found 170 cases of postabortal tetanus with an average mortality rate of 84 per cent to which they added 14 additional cases. The mortality rate among their cases was only 57 per cent. This decrease was thought to be due to the widespread use of large doses of tetanus antitoxin. Tonge[14] in 1947 reported upon a patient who, following normal

delivery, developed a pulmonary embolus on the seventh day and signs of tetanus on the fourteenth postpartum day. She died on the fifteenth postpartum day and *Cl. tetani* were cultured from both the cervix and the pulmonary infarct. He also reported 2 other cases both of which were fatal, giving a mortality rate in this series of 100 per cent. Jelliffe, Walker, and Matthews[5] in 1950 from England reported one postabortal case and 4 postpartum cases, 3 of which were fatal. One patient also had eclampsia. One was fatal on the tenth postpartum day and another on the twelfth. Eastman has stated that during his stay in China he saw one case after delivery by a midwife and heard of another. Single cases have been reported by Milnor,[10] Edwards,[3] Byrne, Duncan,[2] Knight,[6] Thomas,[13] Komaromy,[7] and Mattson and Starkey.[9]

The source of *Clostridium tetani* is generally considered to be unsterile manipulation, instrumentation, or examination. The Tetanus Committee of the Royal College of Obstetricians and Gynaecologists reported in 1941 that cotton and cellulose dressings were important sources of contamination and that the contamination occurred during the final processing after sterilization. This probably is not true today. Deplorable conditions predisposing to tetanus infections have been described as being common in India.[6] Religious customs, superstitions, and traditions are such that education of the people is difficult. The patients of India, lying upon floors made of manure, straw, and dust, are attended only by midwives who do not hesitate to do repeated unsterile examinations. Dirty rags and native medicines are occasionally placed into the vagina either before or after delivery. Thus it is obvious that many women under these circumstances may die of tetanus unattended and without diagnosis.

Our interest in this condition has been stimulated by the occurrence of the following case at the John Gaston Hospital in Memphis, Tennessee. This is the only case of puerperal tetanus that has been treated at this hospital within the past thirteen years.

Case Report

W. B., 18 years old, Negro, gravida iii, para iii, was admitted to the John Gaston Hospital for the first time on June 27, 1953. Her illness had begun three days prior to admission as a discomfort and stiffness of the jaws. This had been a persistent and progressive discomfort with a gradual onset of difficulty in opening her mouth. On the day before admission she had developed stiffness and drawing of the muscles of the neck and back. She was rational and denied having had headache, convulsions, chills, or fever.

Fourteen days prior to admission she had delivered a normal, full-term infant, being attended only by a midwife. The labor and delivery occurred in the home and were accompanied by an unknown number of vaginal examinations. Until the eleventh postpartum day she had had no difficulty. There had been a moderate amount of lochia which became more profuse and foul smelling on the day before admission. Her other two children had also been delivered by a midwife without complications and both were living and well.

Physical Examination.—Her temperature was 101° F., pulse 136, respirations 24, and blood pressure 118/80. She was a well-developed, well-nourished Negro woman. Trismus was present which limited opening the mouth to one-half inch. There was marked nuchal rigidity and mild opisthotonos. There were several small lacerations on the tongue indicating previous trauma from spasm of the jaw muscles. The abdomen was soft and pliable with a smooth, tender mass extending up from the pelvis to just below the umbilicus. The deep tendon reflexes were slightly hyperactive but equal, and the Babinski response was

present bilaterally. There was no ankle clonus. Pelvic examination revealed a thick, foul, reddish-brown discharge from the cervix that was almost closed. The uterus was three times normal size, displaced to the left and acutely tender.

Laboratory Findings.—On admission the hematocrit was 49 volumes per cent, the white blood count was 10,500 cells per cubic millimeter and the urinalysis revealed 15 to 25 white blood cells per high-power field. The blood culture and culture of the cervical discharge taken on admission were reported as negative. A repeat urinalysis on the thirteenth day showed a 1 plus proteinuria, 5 to 11 red blood cells and 15 to 25 white blood cells per high-power field. On the twentieth day the urinalysis was unchanged, the white blood count was 11,850 with 77 per cent neutrophils and 17 per cent lymphocytes. Urine cultures on the twentieth hospital day were reported to yield coliaerogenes, *Streptococcus faecalis,* and Pseudomonas. Blood cultures on the same day were positive for coli-aerogenes, *Escherichia intermedium,* and *Pseudomonas rugosa.* The coli-aerogenes was moderately sensitive to Choloromycetin and resistant to all other antibiotics. A blood culture three days prior to death was negative.

Clinical Course.—During the first twenty-four hours after admission she had increasing hypertonicity of the muscles in general with trismus and opisthotonos becoming much more severe. Also after twenty-four hours she had her first convulsion which was generalized and tonic in nature. Ankle clonus developed on the second hospital day.

During the first week her temperature ranged from 100° to 101.6° F. (rectally). She was extremely hyperirritable, requiring large amounts of sedatives, and convulsions occurred at intervals of approximately twenty-four hours. Her second week was probably the stormiest of her entire hospital course. She developed a moderate paralytic ileus and periorbital puffiness was noticeable. By the end of the second week she appeared generally improved and less irritable. She was rational and took food and fluids adequately by mouth.

The third week was characterized by a temperature curve with daily spikes to 105° F. and higher. Repeat pelvic examination revealed no evidence of abscess formation within the pelvis. Trismus, ankle clonus, and muscle spasms were greatly diminished. On the twenty-first day she was noted to be somnolent and to react slowly. Her temperature continued to soar during the fourth and final week of her hospitalization. A Levine tube was passed to facilitate the intake of food and fluids. Terminally the patient developed vomiting, diarrhea, and a slight degree of generalized edema. Death occurred quietly on the twenty-eighth hospital day.

Treatment.—The patient was placed in a private room with noise and light excluded as much as possible. Suction was provided for the removal of nasopharyngeal secretions.

Initial therapy consisted of aqueous penicillin, 300,000 units every three hours, streptomycin, 0.5 Gm. every six hours, phenobarbital, 1 grain by mouth every six hours, and Tolserol, 1 Gm. by mouth every six hours. Forty thousand units of tetanus antitoxin was given intravenously and 40,000 units intramuscularly as an initial dose with a maintenance dose of 10,000 units intramuscularly daily. Occasionally additional sedation such as Nembutal or Amytal was required to control restlessness, irritability, or convulsions. On the second day the daily antitoxin was increased to 40,000 units. This was maintained until the fourteenth day when it was decreased again to 10,000 units daily. On the twentieth hospital day she was started on Terramycin, 500 mg. every six hours. Intravenous glucose was given from time to time to augment the fluid intake. The Terramycin was changed to Chloromycetin, 500 mg. per Levine tube every six hours, because of a blood culture report positive for coli-aerogenes that was moderately sensitive to Chloromycetin.

Autopsy Findings.—The autopsy findings in a case of puerperal tetanus have never been well described. Duncan[2] reported a case with an adherent piece of placenta as the only significant autopsy finding. Tonge[14] has reported three cases with autopsies, the most consistent findings being an enlarged, friable, hemorrhagic uterus; congestion and consolidation in the lungs; and nothing in the central nervous system. One case had a pulmonary infarct, and cultures taken from the cervix of this patient and from the infarct were positive for *Clostridium tetani.*

An autopsy was performed on our patient six hours after death. At this time she presented the picture of a well-developed, well-nourished Negro woman. The heart weighed 300 grams and showed no specific abnormality. The right lung weighed 280 grams and the left 260 grams. The cut surface of the lungs presented a red fluid and there was diffuse atelectasis of the upper lobes. There was microscopic evidence of moderate congestion and edema with some leukocytic infiltration.

The spleen weighed 260 grams and on cut surface was found to be soft and markedly congested. Microscopically the normal follicular pattern was absent. The sinusoids were extremely dilated and filled with red blood cells. The liver weighed 2,400 grams. The capsule was smooth and the cut surface was dull red with no scarring. Microscopically there was seen to be a rather extensive cloudy swelling of the cells, but no areas of inflammation or necrosis. The kidneys were involved in a rather extensive inflammatory process. The surfaces were seeded with multiple abscesses. The cortices, medullae, and pelves contained multiple foci of abscess formation. The abscess cavities were filled with white cells, cellular debris, and amorphous material. There was marked leukocytic and round-cell infiltration into the interstitial tissue. Marked tubular degeneration was evident.

The uterus was absolutely free of pathological change. It was a normal postpartum uterus with no inflammatory processes. The inner surface was smooth and glistening. Sections from the brain and spinal cord showed absolutely no evidence of pathological changes and there were no meningeal lesions. The final pathological diagnoses were (1) septicemia with bilateral renal abscesses, congestive splenomegaly, and cloudy swelling of the liver; (2) bilateral bronchopneumonia with diffuse atelectasis.

Comment

It is interesting to note that this patient appeared to be recovering from tetanus when she developed bronchopneumonia, diffuse atelectasis, and a resistant septicemia leading to multiple renal abscesses. The point is also well taken that even though broad-range antibiotics are available one should not assume the attitude that it is impossible to die of overwhelming septicemia.

The symptoms of tetanus are produced through the action of the neurotoxin upon the central nervous system. This toxin is produced by the *Clostridium tetani* regardless of the site of entrance of the organism. In this case we have assumed, with some basis for this assumption, that the site of entrance was the postpartum uterus even though the uterine cultures failed to produce the organisms. As a matter of fact, uterine cultures in cases in the literature were commonly negative. It is probable that the organisms were introduced into the uterus by the unsterile examinations of the midwife; the possibility, however, of contamination from the patient's own fecal material cannot be disregarded. Many authors have reported *Clostridium tetani* in the human intestinal tract. Fildes[4] in 1929 reported that the organisms were present in 1 per cent of the feces examined.

One established principle of treatment of tetanus is the débridement of the entrance wound. This does not apply to postpartum or postabortal tetanus. Dilatation and curettage has been advocated by some authors on the basis that it removes necrotic tissue containing the tetanus organisms. This procedure is probably dangerous, produces no benefit, and should not be attempted if puerperal tetanus is thought to exist. Hysterectomy as a means of wound débridement is difficult to evaluate but it, too, is generally considered to be of questionable value. Bush[1] has reported a case in which the endometrium was noted to be normal following a hysterectomy and the patient received no benefit from the procedure. Our patient illustrated the point that hysterectomy in

all probability would have been of no value since at autopsy the uterus was found to be entirely free of inflammatory processes. Mattson and Starkey[9] state that the administration of large doses of tetanus antitoxin is probably the most important factor in treatment. The use of intrathecal antitoxin has been reported by several authors with good results; others, however, have stated that it is dangerous and should not be used. Dietrich has reported deaths of children with symptoms similar to bulbar poliomyelitis following the intrathecal injection of serum. Maclean and Challen[8] report a case of aseptic meningitis following this procedure. In the case reported by Bush no benefit was realized from the intrathecal injection of antiserum.

It is obvious that the prevention of tetanus is far more important than treatment. We have for a number of years administered prophylactic tetanus and gas gangrene antitoxin to all patients with a history of unsterile invasion of the pregnant uterus.

Summary

1. A case of puerperal tetanus complete with autopsy findings has been presented. This patient was an 18-year-old Negro woman who had been delivered at home by a midwife. She developed signs and symptoms of tetanus on the fourteenth postpartum day and died on the thirty-ninth postpartum day.

2. Death came from generalized septicemia with bronchopneumonia and multiple renal abscesses at a time when the patient appeared to be recovering from the tetanus.

3. Records of 210 cases of postabortal tetanus and 114 cases of postpartum tetanus can be found. The mortality rate with few exceptions has remained between 75 and 100 per cent.

4. Probably the most important factor in the management of puerperal tetanus is the use of large doses of antitoxin. Doses as high as 40,000 to 50,000 units per day should not be considered excessive. We do not recommend the use of intrathecal antitoxin.

5. Dilatation and curettage should never be done when puerperal tetanus is suspected and hysterectomy is generally considered of little therapeutic value as a means of removing the source of infection.

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THE PLACENTAL TRANSFER OF ERYTHROMYCIN

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ERYTHROMYCIN is a potent antibiotic which is effective after oral administration, and relatively free from side effects.[1, 2] For such a drug to be useful for obstetrical patients, as in prophylaxis against infection after premature rupture of the membranes, it is desirable not only that adequate maternal blood levels of the antibiotic be readily obtainable, but also that the drug cross the placenta.

Heilman[1] has presented the only data on the placental transfer of erythromycin. He found erythromycin in the cord blood serum of 3 of 4 infants whose mothers had received the drug. Information was not given as to the dosage of the drug the mother received, or the time elapsed between administration of the drug and the securing of blood samples.

The present report gives data on maternal and umbilical cord blood serum concentrations of erythromycin following administration of the drug to women who were delivered either vaginally or by elective cesarean section.

Methods

Thirty apparently healthy women at term were studied. Each was given by mouth, at varying intervals before delivery, either a single dose or multiple doses of erythromycin.* The patients were subsequently delivered either by elective cesarean section or per vaginam after spontaneous labor or elective surgical induction of labor. Samples of maternal venous blood were collected at intervals before, as well as at the time of, delivery. Specimens of umbilical cord blood were obtained by gravity flow from the placental side of the severed cord. When possible, amniotic fluid was also secured. Blood from nonpregnant individuals who had been given the same dose of the drug served as controls. The erythromycin content of the blood serum and amniotic fluid was determined by a modification of the Rammelkamp[3] serial dilution technique. A mixture consisting of a known concentration of group O human erythrocytes and a known concentration of actively growing hemolytic streptococcus (strain C-203) was added to various dilutions of the material to be tested and to known dilutions of an erythromycin standard. The mixtures were then incubated at 37° C. for 24 hours. The ability of the test material to inhibit hemolysis of the red cells by the streptococci could thus be compared with the ability of known concentrations of erythromycin to prevent hemolysis.

*Compressed tablets Ilotycin—Eli Lilly and Company, courtesy of Dr. J. W. Smith and Mr. G. Pittman.

Results

A. Single Dose Regimen.—Eighteen patients received a single dose of 200, 400, or 800 mg. of erythromycin (Table I). Patients 1 to 5 were given 200 mg. of the drug two hours prior to elective cesarean section; patients 6 to 10 received the same dose upon admission to the labor suite in active labor. Two and three hours after the drug had been given, low serum concentrations of erythromycin were found in 6 of the 10 patients who received a single 200 mg. dose; no antibiotic was demonstrated in the remaining 4. In no instance did the drug appear in the cord blood or amniotic fluid with this dose. Higher concentrations in the maternal blood were usually obtained with a 400 mg. dose; but again no erythromycin was found in the cord blood. Furthermore, 2 of 6 patients failed to have assayable concentrations in the maternal serum even with this dose. Patients 17 and 18 received 800 mg. of erythromycin in gelatin capsules. High concentrations of the drug were found in the sera of both patients, but only one specimen of cord blood, that obtained from the infant of patient 17, presented detectable erythromycin.

TABLE I. THE ERYTHROMYCIN CONTENT OF THE MATERNAL BLOOD SERUM, UMBILICAL CORD BLOOD SERUM, AND AMNIOTIC FLUID IN PATIENTS GIVEN A SINGLE DOSE OF ERYTHROMYCIN

				ERYTHROMYCIN (MICROGRAMS PER MILLILITER)					
				MATERNAL SERUM					
				HOURS AFTER ADMINISTRATION					
PATIENT	ERYTHROMYCIN (MG.)	LABOR	DELIVERY	1	2	3	4	CORD SERUM	AMNIOTIC FLUID
1	200	None	Cesarean	–*	0.20†	–*	–*	0.00	0.00
2	200	None	Cesarean	–*	0.02†	–*	–*	0.00	0.00
3	200	None	Cesarean	–*	0.02†	–*	–*	0.00	0.00
4	200	None	Cesarean	–*	0.00†	–*	–*	0.00	0.00
5	200	None	Cesarean	–*	0.00†	–*	–*	0.00	0.00
6	200	Yes‡	Vaginal	0.00	0.40	0.30†	–*	0.00	–*
7	200	Yes‡	Vaginal	0.00	0.00	0.15	0.30†	0.00	–*
8	200	Yes‡	Vaginal	0.00	0.00	0.15†	–*	0.00	–*
9	200	Yes‡	Vaginal	0.00	0.00	0.00	0.00†	0.00	–*
10	200	Yes‡	Vaginal	0.00	0.00†	–*	–*	0.00	–*
11	400	Yes‡	Vaginal	–*	0.80†	–*	–*	0.00	–*
12	400	Yes‡	Vaginal	–*	0.80†	–*	–*	0.00	–*
13	400	Yes‡	Vaginal	0.00	0.00	0.00	0.80†	0.00	–*
14	400	Yes‡	Vaginal	0.00	0.00	0.20†	–*	0.00	–*
15	400	Yes‡	Vaginal	0.00	0.00	0.00	0.00†	0.00	–*
16	400	Yes‡	Vaginal	0.00†	–*	–*	–*	0.00	–*
17	800	Yes‡	Vaginal	–*	2.50	–*	0.60†	0.15	–*
18	800	Yes‡	Vaginal	–*	1.25	–*	1.25†	0.00	–*

*No assay.
†At delivery.
‡Erythromycin given during labor.

B. Multiple Dose Regimen.—Each of 12 patients was admitted to the hospital on the day prior to elective cesarean section or elective induction of labor and given a total dose of 800 mg. of erythromycin according to the following schedule:

400 mg. erythromycin	12 to 17 hours before delivery
200 mg. erythromycin	4 to 6 hours before delivery
200 mg. erythromycin	2 to 4 hours before delivery

Patient 30 received an extra 200 mg. of the drug approximately one hour prior to delivery.

All of the subjects who received erythromycin according to this dosage scheme developed detectable concentrations of the drug in their sera. In 8

of the 12 patients erythromycin could be demonstrated in the cord blood (Table II). Amniotic fluid was obtained from 3 patients, and assayable concentrations of the drug were found in 2.

TABLE II. ERYTHROMYCIN IN MATERNAL BLOOD SERUM, UMBILICAL CORD BLOOD SERUM, AND AMNIOTIC FLUID FOLLOWING MULTIPLE DOSES ADMINISTERED ORALLY BEFORE LABOR

PATIENT	TOTAL DOSAGE OF ERYTHROMYCIN (MG.)	LABOR	DELIVERY	INTERVAL BETWEEN FIRST DOSE AND DELIVERY (HOURS)	ERYTHROMYCIN (MICROGRAMS PER MILLILITER)		
					MATERNAL SERUM	CORD SERUM	AMNIOTIC FLUID
19	600	Induced	Vaginal	12	0.40	0.00	–*
20	800	Induced	Vaginal	14	2.50	0.08	–*
21	800	Induced	Vaginal	17	0.60	0.08	–*
22	800	Induced	Vaginal	16	0.40	0.00	–*
23	800	Induced	Vaginal	19	0.30	0.60	–*
24	800	Induced	Vaginal	13	0.30	0.04	–*
25	800	Induced	Vaginal (twins)	15	0.30	0.00 0.00	–*
26	800	None	Cesarean	12	0.60	0.04	0.04
27	800	None	Cesarean	13	0.60	0.04	0.04
28	800	None	Cesarean	15	1.50	0.08	–*
29	800	None	Cesarean	15	0.30	0.00	0.00
30	1,000	Induced	Vaginal	16	0.20	0.04	–*

*No assay.

Comment

Four of 10 patients who received a single dose of 200 mg. of erythromycin and 2 of 6 patients who received a single dose of 400 mg. failed to have detectable concentrations of the antibiotic in the maternal blood serum at the time of delivery. We have found that similar doses of erythromycin have frequently resulted in detectable concentrations of the drug in the sera of nonpregnant individuals. It appears that there may be factors present in pregnant women at term which interfere with the appearance of the drug in the maternal blood and, hence, in the cord blood. Josselyn and Sylvester have shown that the absorption of erythromycin probably occurs in the upper gastrointestinal tract and is adversely affected by gastric secretions.[4] Delayed gastric emptying, which is considered to accompany active labor, would tend to increase the exposure of the drug to gastric secretion. Stomach emptying may be further interfered with by analgesics employed during labor.[5] Even, however, in the patients who were delivered by cesarean section, and who had had no labor, and had received only scopolamine hydrobromide, 0.4 mg., as preanesthetic medication, 2 of 5 individuals had no detectable erythromycin in their sera two hours after a 200 mg. dose.

All patients who received multiple doses of erythromycin presented detectable concentrations in the maternal blood at the time of delivery. In these patients the drug was given before the surgical induction of labor and over a sufficient length of time to take advantage of a possible cumulative effect. Despite presumably adequate maternal blood concentrations at the time of delivery, no detectable concentrations of erythromycin were found in the cord sera from 4 of 12 patients (Nos. 19, 22, 25, and 29). Patient 19

received only 600 mg. of the drug, and patient 25 delivered twins; patients 22 and 29, however, delivered full-term living children under the same relative conditions as other patients on this dosage regimen.

This study did not evaluate the factors influencing the placental transfer of erythromycin; nor was it adequate to outline the dosage regimen which would ensure antibiotic protection of the antepartum patient with ruptured membranes. It does seem apparent that the most effective maternal blood concentrations of erythromycin, as well as placental transfer of the drug, may be obtained by administering large doses at frequent intervals over a considerable period of time prior to active labor.

Summary

Thirty pregnant women at term were given single or multiple doses of erythromycin. No erythromycin could be detected in the sera of the blood of 6 of 18 patients administered a single dose of from 200 to 800 mg. of the drug. An assayable maternal serum concentration was obtained in each of 12 subjects given a total multiple dose of 600 to 1,000 mg. Detectable placental transfer of the drug, however, occurred in only 8 of the 12. Relatively low concentrations in the maternal blood, and hence in the cord blood, were found even in the absence of labor or the use of analgesics, both of which may interfere with emptying of the stomach.

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REPORT OF THE MATERNITY CENTER ASSOCIATION CLINIC, NEW YORK, 1931-1951*

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A SAFE plan for delivery in the home is presented, and the work of the first twenty years of the Clinic and Midwifery School of the Maternity Center Association of New York is reviewed.

The techniques of obstetrics in the home discussed in this paper are those followed by the Maternity Center Association's Nurse-Midwifery Clinic which was organized in 1932. This clinic is operated by the Maternity Center Association under its medical board. It has a staff of three obstetricians, a medical director and two attendings, eight graduate nurse-midwives, and six or eight nurse-midwife students. The responsibility for the administration of the clinic and school is vested in an experienced nurse-midwife.

For clarity, may I say that these nurse-midwives are graduate nurses who like maternity nursing and prepare themselves for midwifery by taking the six months' course offered at the Maternity Center Association which includes theory and actual practice. These nurse-midwives do all the normal deliveries in the homes, delivery in the complicated cases being done by the attending obstetricians.

The figures I shall give are from this nurse-midwifery service which was conducted at the Lobenstine Clinic on West 113th Street in the early days and more recently at the Berwind Clinic at 125 East 103rd Street.

In 1935 in the United States, 63 per cent of all deliveries were in the home, but by 1951 the percentage of births in the home decreased to slightly over 10 per cent.

From 1932 to the end of 1951 the Maternity Center Association Clinic registered for care 6,884 patients. Of these patients 1,119, or 16 per cent, were transferred to other medical care during pregnancy, because, although they were satisfactory patients for home delivery from the medical point of view, their social and economic conditions were such that home delivery was contraindicated (Table I).

Referral to Hospital.—

From the beginning the plan was to care for normal patients in the home and transfer to the hospital any patient with a complication. The commonest reasons for referral to the hospital have been:

*Presented at a meeting of the Section on Obstetrics and Gynecology of the New York Academy of Medicine, Oct. 27, 1953.

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During Antepartal Period: Toxemia, vaginal bleeding, hyperemesis, acute infectious diseases, pulmonary tuberculosis, cardiac disease, pyelitis.

During Labor: Primiparous breech presentation, uterine inertia, prolonged labor, cervical dystocia, persistent occiput posterior, premature labor, multiple pregnancy, cephalopelvic disproportion, prolapsed cord.

During the Puerperium: Hemorrhage, retained placenta, sepsis.

This study covers the other 5,765 registered patients. Of these, 4,988 were delivered in their homes by nurse-midwives and doctors, 98.8 per cent by nurse-midwives and 1.2 per cent by physicians. The remaining 777 patients were hospitalized for medical reasons (Table II).

TABLE I. TOTAL REGISTRATIONS ACCEPTED FOR HOME CARE BY THE M.C.A. MEDICAL SERVICE

DISPOSITION OF REGISTRANTS		NUMBER		%
Dismissed pregnant (because of social and/or economic reasons, although approved medically for home care)			1,119	16.5
Delivered at home		4,988		72.2
By nurse-midwives	98.8%			
By physicians	1.2%			
Hospitalized for medical reasons		777		
			5,765	11.3
Total registrations			6,884	100.0

TABLE II. TOTAL PREGNANCIES TERMINATED IN HOME AND HOSPITAL

	DELIVERY IN		
	HOME	HOSPITAL	HOME AND HOSPITAL
No. mothers	4,988	777	5,765
No. mothers with multiple pregnancy	55	24	79

Note.—Two mothers who had twin pregnancies, each delivered one twin at home and the other twin in the hospital. The multiple pregnancy of each of these mothers is counted only once in Table II. They are counted in the Home and *not* in the Hospital.

Even with the most careful screening of patients accepted for home delivery during the time the patients were under care, 11.3 per cent required hospitalization in the interest of safety for the mother and/or for her infant. In this clinic service no attempt is made to urge mothers to have their babies at home. Rather, each mother is considered individually on the basis of her combined medical, social, and economic condition, in an effort to help her make a wise and safe choice as to home or hospital delivery.

Frequently during the antepartum service to these mothers the original choice of home delivery was changed to hospital care on account of the patient's changed medical, social, or economic situation.

Delivery of the 5,765 registered patients in home and hospital resulted in 5,846 births as there were 79 mothers who had multiple pregnancies. There were 5,340 spontaneous vertex deliveries, 4,906 in the home and 434 in the hospital; 105 spontaneous breech deliveries, 86 in the home and 19 in the hospital; 60 assisted breech deliveries, 25 in the home and 35 in the hospital; 47 breech extractions, 6 in the home and 41 in the hospital; 136 forceps deliveries, 11 in the home and 125 in the hospital; and 80 cesarean sections (Table III). The results of 2 births in the hospital were not reported. There were 5,627 live infants, 4,955 born at home and 672 in the hospital; 164 stillborn infants, 79 delivered in the home and 85 in the hospital; and 53 early abortions, 10 in the home and 43 in the hospital. Of the mothers who had multiple pregnancies, 55 delivered in the home and 24 in the hospital (Table IV).

TABLE III. METHOD OF DELIVERY IN HOME AND HOSPITAL OF 5,846 BIRTHS

METHOD OF DELIVERY	HOME	HOSPITAL	HOME AND HOSPITAL
Spontaneous vertex	4,906	434	5,340
Spontaneous breech	86	19	105
Assisted breech	25	35	60
Breech extraction	6	41	47
Forceps delivery	11	125	136
Cesarean sections	0	80	80
Not determined	0	25	25
Early abortions	10	43	53
Total births	5,044	802	5,846

TABLE IV. TOTAL BIRTHS (LIVE BIRTHS AND FETAL DEATHS) IN HOME AND HOSPITAL

BIRTHS		HOME		HOSPITAL		HOME AND HOSPITAL
Live births		4,955		672		5,627
Fetal deaths		89		130		219
Stillbirths	79		85		164	
Early abortions	10		43		53	
Not determined	0		2		2	

All of the 5,765 mothers had at least four weeks of antepartum care and over 90 per cent of the mothers had eight weeks or more.

Gravidity.—

Eight hundred twelve, or 14 per cent, of the patients were primigravidas. Six hundred two, or 74 per cent, of these primigravidas were delivered in the home and 210, or 26 per cent, were delivered in the hospital (Table V).

TABLE V. PRIMIGRAVIDAS AND MULTIGRAVIDAS BY HOME AND HOSPITAL DELIVERIES

PLACE	PRIMIGRAVIDAS		MULTIGRAVIDAS		TOTAL	
	NO.	%	NO.	%	NO.	%
Home	602	74	4,386	88	4,988	86
Hospital	210	26	567	12	777	14
Total home and hospital	812	100	4,953	100	5,765	100
Primigravidas					14%	
Second and third pregnancies					40%	
Tenth pregnancy and over					5%	

Of the 4,953 multigravidas, 4,386, or 88 per cent, were delivered at home and 567, or 12 per cent, were delivered in the hospital. Forty per cent were having their second and third babies and 5 per cent were in their tenth pregnancy. The numbers decreased as the gravidity increased, but 268 mothers in their tenth pregnancy were given care.

Economic Status.—

A low-income group is served, but there have been changes even within this group. In 1932 to 1936, 42.6 per cent were dependent, while there were no families with an income of $40.00 per week or over. In 1951 only 22.2 per cent were dependent, while 9.8 per cent had an income of $60.00 per week or more.

Nutrition.—

Poor nutrition has been a problem from the beginning of the Clinic. In 1932 to 1949, 36.4 per cent of the patients showed secondary anemia. The diagnosis was made when the hemoglobin was 9 Gm. or less. In the past two years only 3.6 per cent have shown the same degree of anemia. Since January,

1949, a more detailed study of the diets has been made and an appraisal chart based on recommended allowances by the National Research Council has been used. According to this diet appraisal there seem to be more "good" and fewer "poor" diets in the last trimester than at the time of registration.

All patients are given iron and multiple vitamins throughout pregnancy. Any patient who has a hemoglobin of 8 Gm. or under, who does not respond to dietary advice and to the administration of iron, is referred to the hospital for blood transfusion.

We have had our share of other complications of pregnancy. We have looked after 53 patients with pulmonary tuberculosis. After consulting with the Department of Health Diagnostic Service, we delivered 16 patients with arrested pulmonary tuberculosis in the home and referred 37 to the hospital for care. In the early years of the Clinic service, x-ray of the chest was taken whenever the history or findings suggested the advisability of doing so. Since 1942 all patients have had x-ray of the chest. There has been an incidence of about 1 per cent of pulmonary tuberculosis.

The incidence of syphilis (positive Mazzini test) was 6.3 per cent.

We have attempted to do external podalic version whenever a breech presentation was diagnosed in the last eight weeks of pregnancy. Of the 321 versions attempted, 272 were successful and 49 were unsuccessful (Table VI).

TABLE VI. EXTERNAL VERSION, SUCCESS AND FAILURE IN 5,846 BIRTHS IN HOME AND HOSPITAL

	HOME	HOSPITAL	HOME AND HOSPITAL	
			TOTAL	%
Total attempted versions	285	36	321	100
Successful	251	21	272	84
Unsuccessful	34	15	49	16

Incidence of breech presentation at time of delivery

Home	117
Hospital	95
Total	212

In 5,846 births, this gives an incidence of 3.6 per cent breech presentations at time of delivery.

The incidence of breech presentation at the time of labor and delivery was 3.6 per cent. The incidence at three of the large obstetric services in this city in 1951 was:

New York Hospital	4.2%
Bellevue Hospital	4.6%
Sloane Hospital	4.3%

All patients received instruction about labor and delivery in Clinic, in Mother's Classes, and at the Home Preparation Visit. Some weeks before term each is given a typewritten reminder about when to call the clinic.

WHEN YOU THINK YOUR BABY IS COMING
WRITE ON THIS SLIP:

What time the contractions began.
How often the contractions come.
Have the "waters broken"?
Is there any bleeding?

Give this slip to whoever telephones
the clinic for you.

The arrangements for and the technique of the actual delivery follow those of the modern delivery room, with simplifications. The patient supplies the simple equipment for herself and baby. The Clinic delivery bag and medicine kit provide all other necessary equipment. There is also a bag with equipment for the treatment of complications. A portable oxygen tank and an incubator are readily available. The transfer of patients to the hospital via private ambulance has always been provided for in the Clinic budget, and has been an essential element of safety in the service.

Duration of Labor.—

The average duration of labor was 6 hours, 45 minutes. The average time spent by our staff midwife with each patient was 4 hours, 30 minutes.

Sedatives are given when indicated; potassium bromide with chloral hydrate, Demerol, and Seconal are used chiefly. Ether is available but has been needed rarely; it has not been used since 1942. Novocain, 1 per cent locally, is used for episiotomy and repair of lacerations. In the twenty years in the home deliveries there have been 22 episiotomies, 238 first-degree lacerations, 187 second-degree lacerations and one third-degree laceration. All but the abrasions have been repaired by the attending obstetricians.

Other complications of labor have not been absent. Premature delivery (28 to 38 weeks) occurred in 293 cases. In the first ten years of the service all infants under 5½ pounds were transferred via incubator-carrier to a premature nursery. We were not satisfied with the number of these infants who survived. Since 1944 any patient who goes into labor when the fetus appears to be under 5½ pounds is transferred to the hospital for delivery. During a recent study of our premature deliveries an interesting fact emerged. Labor and delivery in almost all of these patients had occurred after the first clinic visit. That is, they had had no antepartal care. The incidence of premature labor was 6 per cent.

There have been 110 patients with intrapartum uterine inertia (Table VII). As we never use Pitocin in the first or second stage of labor, inertia can be a very annoying complication. Patient, family, and attendants all grow weary. Fifty of these patients were delivered safely in the home, 60 were hospitalized.

TABLE VII. COMPLICATIONS OF LABOR*

COMPLICATIONS	HOME	HOSPITAL	HOME AND HOSPITAL
Premature ruptured membranes	778	262	1,040
Cervical dystocia	6	20	26
Uterine inertia, intra partum	50	60	110
Uterine inertia, third stage	16	3	19
Tetanic uterus	1	0	1
Contraction ring	0	6	6
Prolonged labor	23	72	95
Multiple pregnancy	55	24	79
Placenta previa	6	26	32
Premature separation of placenta	3	49	52
Prolapsed cord	10	21	31
Cord presentation	1	0	1
Retained placenta	13	29	42
Postpartal blood loss, 500 c.c. and over	214	71	285
Impacted shoulder	7	10	17
Cephalopelvic disproportion	7	10	17
Irregular fetal heartbeat	6	10	16
Other	13	55	68
Mothers with no complications	2,782	245	3,027
Mothers with complications	2,206	532	2,738
Total	4,988	777	5,765

*Other complications of labor not included in this list were precipitate labor, laceration of the perineum, episiotomy, and laceration of the cervix. These totaled an additional 1,709 patients with complications.

We have had 42 patients with retained placenta, i.e., the placenta was not delivered after one hour or more. In 13 patients the blood loss was under 500 c.c., the placenta was finally expressed, and the condition of the patient remained good. Twenty-nine patients with retained placenta were transferred to the hospital.

Postpartum hemorrhage is the greatest single worry in a home delivery service. Our incidence of blood loss of 500 c.c. and over in the home is 4.3 per cent. If the bleeding can be readily controlled and the patient shows no sign of shock, she may remain at home. We give infusions of dextrose in the home, but as most of these patients need replacement of blood, they are transferred to the hospital for transfusion. There has been no death from postpartum hemorrhage.

These complications have occurred in spite of every effort to keep blood loss at a minimum. Clots and fluid blood are measured after delivery. Up to the end of 1950 oxytocics were used only when indicated after the end of the third stage. Beginning Jan. 1, 1951, all patients received pitocin, 1 c.c. hypodermically, and Ergotrate, 0.0002 Gm. hypodermically after the third stage. In spite of the small numbers involved, there appears to be some decrease in blood loss.

In the 4,988 home deliveries we had a morbidity rate of 2.5 per cent (126 patients morbid). The total rate, home and hospital, was 3.8 per cent.

TABLE VIII. BIRTHS AND FETAL, NEONATAL, AND MATERNAL DEATHS BY NUMBER AND RATE

	HOME	HOSPITAL	TOTAL HOME AND HOSPITAL	RATES* PER 1,000 BIRTHS	RATES* PER 1,000 LIVE BIRTHS
Total births†	5,044	802	5,846		
Live births	4,955	672	5,627		
Fetal deaths	89	130	219	38	39
Neonatal deaths	50	34	84	14	15
Maternal deaths	0	5	5	0.86	0.9

*Gross fetal and neonatal death rate per 1,000 births, 52.0. Gross fetal and neonatal death rate per 1,000 live births, 54.0.

†Includes multiple births: at home 56, in the hospital 25, total 81.

Five patients have died after transfer to the hospital on account of serious complications (Table VIII). This is a maternal mortality rate of 0.88 per 1,000 live births or 0.86 of the total births; 5 in 5,765 deliveries (Table IX).

TABLE IX. MATERNAL DEATHS

YEAR	DIAGNOSIS
Deaths Due to Pregnancy, Delivery, and Postpartum Conditions.—	
1933	Puerperal sepsis
1937	Placenta previa
1938	Premature separation of placenta
Deaths Due to Underlying Causes Rather Than to Childbearing.—	
1945	Stenosis of the larynx due to fibrosis (autopsy report)
1951	Intracranial hemorrhage (autopsy report)

All patients are visited in the home by the nurse-midwives during the first ten days after delivery, and come to the Clinic for medical supervision at the end of two and six weeks post partum. The infants are referred to Baby Health Stations and 80 per cent are registered by 6 weeks of age.

Diet appraisals carried out at this time show a higher percentage in the "good" group.

In these 20 years we have had 5,627 live births, 219 fetal deaths, and 84 neonatal deaths. Thus we have a fetal death rate of 38 per 1,000 births, or 39 per 1,000 live births; and a neonatal death rate of 14 per 1,000 births or 15 per 1,000 live births. In this group there was a high incidence of poor nutrition, poor home conditions, low income, unmarried mothers, and high parity. In spite of this our neonatal death rate is much lower than the rate for the whole Clinic area.

Conclusions

1. Under the conditions which obtain in this Maternity Center Clinic service, deliveries can be conducted safely in the home.

2. Arrangements for rapid transfer of patients with complications to an interested hospital obstetrical service are essential.

3. Patients with parity of viii or over should be hospitalized.

4. Patients in premature labor should be hospitalized as soon as possible.

5. Routine oxytocics should be employed following the third stage.

6. Nutrition appraisals followed by adequate education and interpretation show encouraging results. Iron and vitamin supplements are given as needed.

7. Fetal and neonatal loss can be decreased by better and individual care and perhaps by the improvement in nutrition already mentioned.

8. The average length of labor was short. This may be due to the confidence engendered in the patient and her family by the satisfying personal contact in this small service. Patients were attended by the nurse-midwife an average of four hours, thirty minutes, during the average labor of six hours, forty-five minutes.

One cannot have been associated with such a service for over twenty years, as has been my privilege as a teacher and clinician, without pondering these questions:

Is there something about this service which might be transferred to the hospital scene to attract well-qualified, serious-minded nurses and keep them in the field of obstetrics?

Are there some very simple lessons to be learned from the relationships of the doctor, nurse, and family in the home that might help to achieve in the hospital a better and more satisfying relationship?

Can this more intimate, friendly way of teaching people, which is carried on in the Clinic and in the homes, show us something about teaching in the hospitals?

I wish to express my gratitude to the Director and Staff of the Maternity Center Association Clinic for their valuable assistance in the preparation of this report.

POSTPARTUM MANUAL INTRAUTERINE EXAMINATION

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THE primary purpose of this study is to determine the relationship of morbidity to elective intrauterine examination immediately following the third stage of labor.

In the course of reviewing records, it was considered advantageous to chart all temperatures elevated above 100° F.; to note the relationship to concomitant use of antibiotics; to evaluate the incidence of postpartum hemorrhage associated with retained secundines; to note the patients who passed more than the usual lochia in the postpartum period; and finally to tabulate all patients who evidenced no morbidity, hemorrhage, or elevated temperatures, and who received no antibiotics. We shall include in this study complications noted as a result of this procedure.

As a control study, an equivalent number of cases prior to the date of initiation of this routine was also critically reviewed with consideration of all the above points.

We are acutely aware of the time-honored dictum of ". . . no meddlesome midwifery. . . ." We are cognizant of the hazards associated with a procedure of this type. The observations of Te Linde that every uterus is probably infected in the postpartum period regardless of the extent of aseptic technique do not fall upon deaf ears. His statement that an elevated temperature with or without leukocytosis is not a necessary criterion of infection has been seriously considered.

Our observations, however, point to the conclusion that this procedure, practiced diligently, is an innocuous one; and that the benefits to be derived if only one life is salvaged far outweigh the possible hazards, which are probably of academic interest only, if sterile technique is followed minutely.

Technique

The procedure presupposes an absolutely sterile technique. Following delivery of the placenta, the hand is carefully introduced into the uterus. The organ is examined minutely for tears and rents, retained secundines and cotyledons, and for any other intrauterine pathology. Note is made of the tonus of the uterus, its movability, station, and the presence of congenital anomalies. Of course, full evaluation of the cervix is accomplished with this procedure on removal of the examining hand. Extreme care must be taken to eliminate anal contamination.

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TABLE I. CASES OF MORBIDITY

CASE	POSTPARTUM DAY 1	2	3	4	5	6	7	8	AFTER 8	ANTIBIOTIC	LABORATORY TESTS AND URINE	BREAST FED	DIAGNOSIS AND REMARKS
A. Test Series.—													
1			101	101					Home on 9	Third day	Neg.	Yes	Episiotomy infection
2							103	102	Home on 10	Seventh day	50 wbc	No	Pyelitis
3							103	102	Home on 13	Seventh day	40 wbc	Yes	Pyelitis
4	102	101		100					Home on 9	First day	Neg.	No	Endometritis
5	Spiking temperatures throughout									Second day	Blood smear positive for infectious mononucleosis		
B. Control Series.—													
1		102		101					Home on 9	None	30 wbc	Yes	Pyelitis
2	100	101	103	100	101	100			Home on 11	Third day	20 wbc	Yes	Cystitis
3			105	101	100	99	99		Home on 13	Third day	90 wbc	No	Pyelitis
4				102	101				Home on 8	None	Neg.	Yes	Endometritis
5	100	102	103	103	102				Home on 8	Fourth day	Neg.	No	Endometritis
6	101	102	101	101	101	101	101		Home on 16	Third day	40 wbc	Yes	Pyelitis
7		102	101	100	Home					None	20 wbc	No	Pyelitis
8				101	100				Home on 9	Fourth day	Neg.	No	Breast engorgement
9				102	103	100			Home on 10	None	Neg.	No	Breast engorgement
10	105	101	102	103	101		Home			First day	X-ray	No	Pneumonia
11			102	103			Home			Fourth day	Neg.	No	Breast engorgement
12		101		100	101		100		Home on 12	Second day	X-ray pos.	No	Bronchitis
13			102	103	103	102	101		Home on 10	Third day	90 wbc	No	Pyelitis

Clinical Material

The study covers the period from Jan. 15, 1949, to Aug. 15, 1951. The first date is chosen because it was then that the senior author* commenced routine intrauterine examination following detection of a rupture of the uterus in a patient who had completed a perfectly uneventful delivery. The latter date is an arbitrary one, as the material available for study could be obtained only up to that date.

In order best to evaluate the problems, only the private patients of the senior author have been included. Five hundred ten consecutive deliveries are represented but cesarean sections are excluded.

The control study includes a critical review of 500 cases from Sept. 1, 1946, to Jan. 15, 1949, and again represents consecutive deliveries excluding cesarean sections.

Our definition of morbidity is the one accepted by the American Committee on Maternal Welfare, "... a temperature of 100.4° or over on any two postnatal days following the first 24 hours through the tenth postnatal day. ..." Of course, our study falls somewhat short in that there were very few patients who remained in the hospital for the full ten-day period. We cannot attempt to ascertain how many of these were morbid after discharge.

Morbidity Cases.—

It will be noted that morbidity temperatures occurred in only 5 patients, none of whom received antibiotics prior to the elevation of temperature. This translated into percentages means an over-all morbidity of only 0.98 per cent. Only one of these cases, however, was considered to be postpartum endometritis. This then gives a corrected morbidity rate of 0.19 per cent as possibly due to intrauterine manipulation. Table I, A lists the cases mentioned.

In the control series (Table I, B), there were 13 patients who had morbidity temperatures. None of these patients received antibiotics prior to the elevation of temperature. This gives an over-all morbidity rate of 2.6 per cent. Cases 4 and 5 were adjuged to be endometritis. The corrected morbidity rate referable to the uterus then was 0.4 per cent. This figure is to be compared with the rate of 0.19 per cent in the test series. The morbidity rate in the test series was therefore less than in the control series.

Nonmorbidity Temperature Elevations.—

In the test group there were 4 cases that could critically be considered as possible endometritis, and probably the immediate use of antibiotics prevented morbidity. Of these 4, only one could be definitely diagnosed as endometritis. The corrected percentage of nonmorbidity temperature elevations, which could possibly be due to intrauterine manipulation, then, is 0.19 per cent, if only the one case is considered. If all 4 cases are included, the incidence is 0.79 per cent. In this group, there were 31 nonmorbidity temperature elevations.

In the control group, there were 45 nonmorbidity temperature elevations. Three cases were adjudged to be early endometritis, and there were 9 cases which could be considered as possibly early endometritis. The nonmorbidity temperature elevation rate for the control series then is 2.3 per cent.

Analysis of these two groups then shows that there were fewer temperature elevations (nonmorbidity) in the group that had intrauterine manipulation than in the control group, as evidenced by the incidence of 0.79 per cent in the test group as compared to 2.3 per cent in the control group.

*Donald Snyder, M.D.

Patients Who Received Antibiotics but Had No Elevation of Temperature.—This review is very difficult to evaluate as all the patients in the test group, except 2, were given antibiotics for other conditions. These 2 did pass foul lochia, so that we may consider them as aborted cases of endometritis. Thus the sum total of known cases of endometritis, which includes the known morbidity case in Table IA and the one case in the nonmorbid test group, plus the 2 cases listed above, brings the number to 4, or an over-all incidence of 0.76 per cent.

The difficulty of evaluation of this study lies in the question that presents itself, "How many of these patients would have developed endometritis if antibiotics had not been given?" There were 50 patients in the test group who received antibiotics, 2 of whom passed foul lochia, while in the control group there were 17 patients, none of whom passed foul lochia.

Patients With Postpartum Hemorrhage or With More Than Usual Lochia.—It is the established custom of the hospital that all clots expressed are brought to the attention of the House Staff or the attending physician. Any increase in the amount of flow of lochia is indication for notification of the resident or staff man.

In Table II, *A*, note that in spite of intrauterine examination, abnormal passage of clots and tissue occurred. If fragments could be left in even after a careful examination, we feel it is fair to assume that without examination there is very frequently tissue left in the uterus.

In the control series, there were 8 cases where retained placenta was the cause of postpartum bleeding. It may be noted that there were 33 cases of retained placenta which were discovered with intrauterine examination.

TABLE II. PATIENTS WITH POSTPARTUM HEMORRHAGE AND/OR WHO PASSED PLACENTAL TISSUE

CASE	REMARKS
A. Test Series.—	
1	Following return to postnatal room, hemorrhage noted. This was due to uterine inertia. Tonus of uterus was very poor. Oxytocics remedied situation
2	Uterine inertia
3	Hemorrhage 10 days post partum. Curettage done, but no tissue
4	Uterine inertia
5	Passage of placental fragment 5 days post delivery
6	Passage of large clots on sixth postdelivery day. Not determined whether this was placental tissue
B. Control Series.—	
1	Postpartum bleeding from episiotomy
2	Postpartum bleeding from episiotomy
3	Postpartum uterine atony with hemorrhage
4	Postpartum uterine atony with hemorrhage
5	Postpartum uterine atony with hemorrhage
6	Postpartum uterine atony with hemorrhage
7	Retained placental fragments
8	Retained placental fragments
9	Retained placental fragments
10	Retained placental fragments
11	Retained placental fragments
12	Retained placental fragments
13	Retained placental fragments
14	Retained placental fragments
15	Postpartum bleeding, cause unknown

Complications Discovered as a Result of Examination.—
The following complications were noted as a result of the intrauterine examination:

1. Rupture of uterus (1),
2. Retention of placental cotyledons (33),
3. Submucous fibroids (4),
4. Retention of membranes, partial (indeterminate number),
5. Uterine inertia. This was noted 3 times in markedly obese women in whom it was difficult to palpate the uterus abdominally.

Summary (Table III)

1. A consecutive series of 510 deliveries dating from Jan. 15, 1949, to Aug. 15, 1951, is analyzed. A control group of 500 deliveries from January, 1946, to January, 1949, is also analyzed.

TABLE III. ALL KNOWN AND POSSIBLE CASES OF ENDOMETRITIS

	TEST GROUP		CONTROL GROUP	
	KNOWN CASES	INCLUDING DOUBTFUL	KNOWN CASES	INCLUDING DOUBTFUL
Morbidity rate	0.19%	0.19%	0.40%	0.40%
Nonmorbidity temperature elevation rate	0.19%	0.79%	0.60%	2.30%
Antibiotics and no temperature elevation	0.39%	0.39%	0.00%	0.00%
Over-all "endometritis rate"	0.77%	0.37%	1.00%	2.70%

2. A simple technique of intrauterine examination is discussed.

3. In the test series, there were 5 cases of maternal morbidity, only one of which was considered as due to intrauterine manipulation. This gives a morbidity rate of 0.19 per cent. In the control series, there were 2 known cases of endometritis with a morbidity rate of 0.40 per cent. Thus the morbidity rate of the test series is less than that of the control series.

4. Analysis of test group nonmorbidity temperature elevation shows one known case, giving an incidence of 0.19 per cent. In the control group there were 3 known cases giving a percentage of 0.60. If in the test group, the doubtful cases are included, the number is 4, with an incidence of 0.79 per cent. If the doubtful cases are included in the control group, there would be 12, with an incidence of 2.3 per cent.

5. There were 50 patients in the test group who received prophylactic or therapeutic antibiotics, and who evidenced no temperature elevations. There were two cases in this group of possible early endometritis, giving a rate of 0.39 per cent. There were no known cases in the control group.

6. If all known cases of endometritis in the test group are tabulated, there is an "endometritis rate" of 0.77 per cent. In the control group, the rating is 1 per cent.

7. If all known and suspected cases are tabulated in each group, we have a test group rating of 1.37 per cent and a control group rating of 2.7 per cent.

8. In the test group, there were 6 cases of hemorrhage and/or passage of placental tissue or clots. Three were due to retained tissue and 3 were due to uterine inertia. In the control group, there were 15 cases of postpartum hemorrhage, in 8 of which placental fragments were passed, plus 4 cases of uterine atony.

9. The immediate benefit to be derived from the procedure is the early detection of: (a) rupture or damage to the uterus, (b) retention of cotyledons or membranes, (c) intrauterine pathology, (d) uterine inertia.

10. Before adoption of routine intrauterine examination, the curettage rate was about 2 per cent. Since adoption, the incidence is less than 0.5 per cent.

Conclusions

1. We feel that intrauterine examination immediately following the third stage of labor is a valuable addition to the obstetrical armamentarium, if the operator is skilled.

2. The principle of asepsis must be rigidly adhered to, as this procedure can be an extremely dangerous one.

3. Again we repeat that "meddlesome midwifery" is not to be condoned, but that the procedure described, scrupulously followed, may well salvage one or two lives in an obstetrician's career.

Department of Case Reports New Instruments, Etc.

EARLY REMOVAL OF THE CORPUS LUTEUM OF PREGNANCY

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EXCISION of the ovary containing the corpus luteum of pregnancy before placental function is established generally has been regarded as a threat to the life of the embryo. In opposition to this view, the function of the corpus luteum in preserving early pregnancy has been questioned. At least two authors[6, 7] doubt its necessity. Recently Glasser[2] has written a good review of the subject. Since there are differences of opinion on the problem and since only a few reports concerning it have been published, I consider the following observations worth recording.

Case History

A 22-year-old, white nullipara, No. 14042, was admitted to the hospital on Nov. 14, 1952, because of severe left lower quadrant abdominal pain of six hours' duration. The patient had suffered intermittent attacks of this pain in a milder form during the preceding six months. Pelvic examination revealed a tender left adnexal mass and slight enlargement of the uterus. A Friedman test was positive. The pain persisted in spite of rest and sedation. After consultation operation was considered advisable because of the constant pain and the size of the mass.

At laparotomy, the left ovary was found replaced by a tense, purplish mass approximately 8 cm. in diameter. A long pedicle and the surface congestion indicated recent torsion. The right ovary was firm and smooth. The uterus was slightly enlarged. The left adnexal mass was completely removed because of its size and congestion and the lack of evidence of any normal ovarian tissue. The pathologist's report was simple cyst of the ovary with a flattened corpus luteum cyst against one of its walls. The external surface revealed dilated and tortuous blood vessels with hemorrhages along their course. The cyst was lined with thecal cells. The corpus luteum was demonstrated microscopically.

The patient's postoperative course was uneventful. She received 25 mg. of progesterone intramuscularly for the first nine days after operation and 12.5 mg. daily thereafter until the fourth month of pregnancy. She also took 10 mg. of diethylstilbestrol daily until the eighth month of pregnancy. She later delivered a healthy male infant that weighed 8 pounds, 1 ounce.

Pertinent data in regard to the length of the pregnancy at the time of the removal of the corpus luteum are as follows:

Onset of last menstrual period	Oct. 2, 1952
Date of operation	Nov. 17, 1952
Date of delivery of infant	July 25, 1953
Time from onset of last period to operation	46 days
Estimated time from period to conception	14 days
Estimated duration of pregnancy at operation	32 days
Average duration of pregnancy after last period	280 days
Duration of this pregnancy after operation	250 days
Estimated duration of this pregnancy at operation	30 days

Comment

The case presented in this report affords another illustration of the fact that pregnancy may proceed normally after the corpus luteum has been removed in the first trimester. Greenhill[3] has estimated that 75 to 100 mg. of progesterone must be given daily to expect any effect in preventing abortion in individuals with low pregnanediol titers. Therefore the 25 mg. and 12.5 mg. daily doses used in this case probably had little effect on the outcome for a patient who had lost the entire corpus luteum of pregnancy. Likewise, no proof exists that the 10 mg. daily doses of diethylstilbestrol were of any value.

The literature contains conflicting opinions on the need for such replacement therapy. Glasser[2] believes that progesterone and estrogen should be given these patients because they may prevent the loss of pregnancy. Michaels[9] has expressed a similar view. On the other hand, several authors have different attitudes. Gruenwald[4] reported upon a patient who had the corpus luteum removed forty-three days after the last period and later delivered a normal term infant. No hormones were administered. Bonn[1] reported a case of removal of both ovaries fifty days after the last period. The pregnancy proceeded without progesterone or estrogen therapy to a term delivery by cesarean section. In an editorial comment on this case, Greenhill *(1948 Year Book of Obstetrics and Gynecology)* stated, "It is almost certain that all ovarian tissue may be removed without disturbing pregnancy." In addition, he cited the work of Hartman and Corner, who found that in the monkey the corpus luteum of pregnancy may be removed as early as the twenty-fifth day of gestation without interrupting pregnancy.

In 1927, Pratt[7] reported upon a patient who had the corpus luteum removed thirty days after her last period and who later delivered a normal baby two hundred seventy-nine days after that period. In the same lecture he reported another case in which the corpus luteum was removed twenty days after the last period and a term infant was delivered two hundred seventy-two days after that menstruation. As far as I can determine, this represents the earliest removal of the corpus luteum of pregnancy which has been reported in the American literature. Neither of these patients received any hormone therapy after operation. In his presentation Pratt also referred to other cases in the literature of early removal of the corpus luteum of pregnancy without any harmful effect. From his study Pratt concluded that there is considerable doubt about the importance of the corpus luteum for successful implantation of the ovum. He further concluded that the danger of abortion following an operation involving the corpus luteum has been exaggerated since it is generally known that abortion may follow any operation on the pregnant individual.

More recently Melinkoff[6] openly doubted that the corpus luteum has any value in maintaining pregnancy and argued that there is no need for replacement therapy. He presented another case of delivery at term following removal of the corpus luteum forty-one days after the last period.

In a very recent study of ovarian tumors in pregnancy Gustafson[5] had two patients from whom the corpus luteum was removed in the first trimester. Both patients went to term. One did not receive any hormones; the other was given 10 mg. of progesterone daily after operation.

Although reports such as those presented previously are in the literature, Williams[8] says, "From the reported cases of ovarian ablation it may be stated that ovaries are absolutely necessary for the maintenance of pregnancy for about four weeks following implantation, for about two weeks more relatively indispensable." This statement simply emphasizes the conflicting opinions on the subject.

Summary

1. A case has been reported of removal of the corpus luteum of pregnancy forty-six days after the last menstrual period. The patient delivered a normal infant two hundred fifty days later.

2. In view of the repeated reports of such patients going to term I doubt the need of the corpus luteum for the maintenance of early pregnancy and question the value of replacement hormone therapy for these patients if that tissue is inadvertently removed during the first trimester.

Thanks are due Dr. Elgin Kintner for the pathology report and the Armed Forces Medical Library for assistance in preparing the list of references.

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A CASE OF INTERSTITIAL PREGNANCY WITH PERFORATION AND EXTENSIVE INTRA-ABDOMINAL HEMORRHAGE MANAGED VIA THE VAGINAL APPROACH

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SINCE interstitial pregnancy is an extremely rare condition occurring, according to Thunig,[1] once in from 2,000 to 6,000 pregnancies, there is justification for reporting this case, particularly since it was successfully managed via the vaginal route.

Of late, surgery by the vaginal approach through the cul-de-sac of Douglas has gained in popularity. Babcock,[2] in 1932, mentioned the feasibility of removing small uterine tumors and ovarian cysts, as well as the vermiform appendix, through the cul-de-sac of Douglas. He stated that for many years he had used this approach in operating for ectopic tubal pregnancy. More recently, Allen[3] and his group in Chicago wrote of their experience with colpotomy in the management of ectopic tubal pregnancy.

Beginning in early 1953, we at The City Hospital of Akron, as well as Peoples Hospital of Akron, have promoted, as part of our residency training in the Department of Obstetrics and Gynecology, an extension of surgery by the vaginal approach to include diagnosis and definitive treatment for ectopic tubal pregnancy. To date, 12 ruptured ectopic tubal pregnancies have been operated upon and several myomectomies and ovarian cystectomies have been performed through the cul-de-sac of Douglas with very satisfactory results. It has been most revealing how easy it is to execute salpingectomy for ectopic tubal pregnancy through the colpotomy incision. These patients have little or no discomfort following this short surgical procedure usually not attended by morbidity. There have been no complications and all patients have been able to care for themselves after the first twenty-four hours and have been ready for discharge by the third to sixth postoperative day. Subsequent follow-up examinations have revealed essentially negative pelvic findings. Two of the patients, upon whom salpingectomy for ruptured ectopic tubal pregnancy had been done, have subsequently presented themselves with normal intrauterine pregnancies. One of our patients had had a previous ruptured ectopic tubal pregnancy managed in the classical manner by laparotomy. This young woman took the trouble to let us know by an unsolicited testimonial how much more comfortable she was in the postoperative course, after the vaginal approach than after the abdominal approach.

The technique that we have followed is that presented by Allen.[3] The entire operative procedure can be completed in less time than is usually necessary to close a laparotomy incision.

Case Report

Mrs. A. M. G., aged 32 years, para i, gravida ii, Unit Number 94003, Peoples Hospital of Akron, was admitted on Sept. 17, 1953, having been referred by her physician as having a possible threatened abortion or ectopic tubal pregnancy. This patient had been considered pregnant and was treated with intravenous pyridoxine for her intractable nausea and vomiting. The last normal menstrual period occurred July 26, 1953, and there had been no bleeding or spotting since that date. On Sept. 12, 1953, however, five days before admission, the patient began to complain of "gas pains" from which she could get no relief from soda bicarbonate or from enema. The next day, September 13, Mrs. G. experienced a sharp knifelike pain in the lower abdomen which subsequently resulted in generalized soreness. She stated that from that time on there had recurred severe cramplike pains in the region of the uterus. The evening of September 14, while attempting to defecate, Mrs. G. fainted and was removed from the bathroom floor by her husband. After recovering, the patient noticed more extreme soreness over the entire abdomen and complained of shoulder pains as well. The latter prevented the patient from taking a deep breath. Subsequent to admission, there had been two more episodes of fainting. There had been no bowel movements nor passage of gas for a period of forty-eight hours prior to admission.

When first seen, the patient appeared pale and her breathing was rapid and shallow. The abdomen was slightly distended, held rigid, and even light palpation was attended with excruciating pain, both direct and rebound. The pulse was rapid and somewhat feeble, the blood pressure 100/60, and the temperature 101.6° F. Pelvic examination revealed a multiparous introitus, a conical, soft, and dusky-appearing cervix, and a uterus corresponding in size to the period of amennorrhea, that is, about the size of a 2½ months' pregnancy. There was a bulging in the cul-de-sac of Douglas and motion of the cervix was attended with severe pain. Because of the discomfort associated with pelvic manipulation, it was impossible to outline the adnexa. I did not, however, palpate any large masses in the region of either adnexa.

The patient's hemoglobin was 7.5 Gm., the red blood count was 2.5 million, and the urine was normal.

A tentative diagnosis of ruptured ectopic tubal pregnancy with intra-abdominal hemorrhage was made.

Blood typing and cross-matching were instituted and the patient was prepared for immediate operation. Blood transfusion was started when the patient arrived in the operating room and under gas anesthesia a calpotomy was performed, through which a tremendous amount of old liquid and clotted blood was released under pressure.

After visual inspection of the right and left adnexa, bringing these structures through the vaginal incision with the aid of sponge forceps and finding them to be normal, we were at a loss to determine the origin of the intra-abdominal hemorrhage. The enlarged uterus was manipulated with considerable difficulty, but was finally tipped backward by a hand-over-hand maneuver with single-toothed tenacula so that the left cornual end was visualized. Here, a bluish-black fragmented clot measuring about 4 by 6 cm. was seen to be protruding from the surface of the uterus and was immediately identified as a ruptured interstitial pregnancy. An elliptical incision was used to remove the clot which contained the intact fetal sac and placenta, and the defect was closed with multiple interrupted No. 00 chromic sutures. The cornual end of the left tube was ligated. The uterine defect having been closed and hemostasis having been affected, the uterus was replaced in its normal anterior position and the calpotomy incision closed in the classical manner. The uterosacral ligaments, which had been previously clamped, severed, and ligated to enlarge the vaginal incision, were reattached prior to closing the vaginal incision.

Two pints of blood were given to the patient before she left the operating room and two additional pints within the next six hours. She was walking after eight hours and was allowed bathroom privileges within twenty-four hours. There were no postoperative complications. On the second postoperative day, the hemoglobin determination was found to

be 11 Gm. per 100 c.c. The patient complained of uterine cramps on the third and fourth postoperative days, which were relieved when she passed an intact decidual cast. There was no morbidity and the patient was discharged on the sixth postoperative day.

Follow-up examination on July 16, 1954, revealed normal pelvic organs and the patient had no complaints referable to the pelvis.

Summary

1. Interstitial pregnancy is a rare condition which occurs about once in from 2,000 to 6,000 pregnancies.

2. Colpotomy appears to be an easy and practical approach for diagnosis and definitive treatment of ruptured ectopic tubal pregnancy.

3. A case of early ruptured interstitial pregnancy was diagnosed and successfully managed via the vaginal approach through the cul-de-sac of Douglas.

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RUPTURE OF RUDIMENTARY HORN OF UTERUS BICORNIS UNICOLLIS WITH PREGNANCY OF 4½ MONTHS*

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THE paucity of reports of pregnancy in the rudimentary horn of a uterus bicornis unicollis, implying the rare occurrence of this condition, has prompted the recording of the following case.

Case Report

Mrs. F. C., 35 years old, white, married, para i, gravida ii, abortions 0, was admitted to the Gynecological Service of the Gouverneur Hospital at 11:00 P.M., Sept. 26, 1952, with the following history:

Beginning at 1:00 P.M. on the day of admission, she had noted a gradual onset of constant lower abdominal pain, which was localized to the midabdomen and epigastrium. It was not very severe and was described as being "somewhat like indigestion." Immediately after the onset of pain, she felt weak and dizzy. She could not stand up because of this, and, when she lay down, she noticed pain in the right shoulder. The symptoms remained unchanged, except that her weakness increased until she was seen by her doctor who sent her to the hospital.

Her last menstrual period had occurred on April 25, 1952. She had experienced all the symptoms of early pregnancy. There had been some brownish red vaginal discharge for one week prior to admission.

There had been no previous operations and no serious illnesses in the past. Her only previous pregnancy, occurring five years before, had terminated in a normal delivery.

Examination showed the patient to be in shock, the skin being cool, clammy, and pale, the blood pressure 60/40, pulse 140 and thready, and the temperature 97.2° F. She was alert and did not seem to be in severe pain. The abdomen was soft with no guarding, but there was some tenderness to pressure followed by rebound tenderness in the right lower quadrant.

On bimanual examination, the uterus was found anterior and slightly enlarged, with marked tenderness elicited on motion. The cervix was soft and a slight dark red discharge was coming from the os. There was a freely ballotable mass of indeterminate size in the cul-de-sac. The hemoglobin was less than 6 Gm., the hematocrit 18 per cent, and the urinalysis was negative. A diagnosis of ruptured ectopic pregnancy was made.

At laparotomy a bicornuate uterus was discovered, the left cornu of which appeared to be rudimentary and connected with the normal right horn by a pedicle about 3 cm. in diameter. The left broad and round ligaments arose from the posterolateral surface of this structure, both tubes and ovaries appearing normal. There was a 6 cm. rent across the anterior surface of the horn from which protruded a mass of placenta, to which was attached the umbilical cord of a 4½ month fetus. The latter was lying free in the abdominal cavity. The rudimentary horn was removed by clamping, cutting, and ligating the pedicle, and the left tube, round ligament, and uteroovarian ligament. The latter

*Presented at the resident's meeting of the Section on Obstetrics and Gynecology at the New York Academy of Medicine, May 26, 1953.

structures were joined to the right horn of the uterus. An estimated 1,500-2,000 c.c. of blood was removed from the peritoneal cavity and a transfusion of 2,000 c.c. of whole blood was given.

Fig. 1.—Removed horn showing fibroid, and the rent from which is protruding placenta, umbilical cord, and fetus.

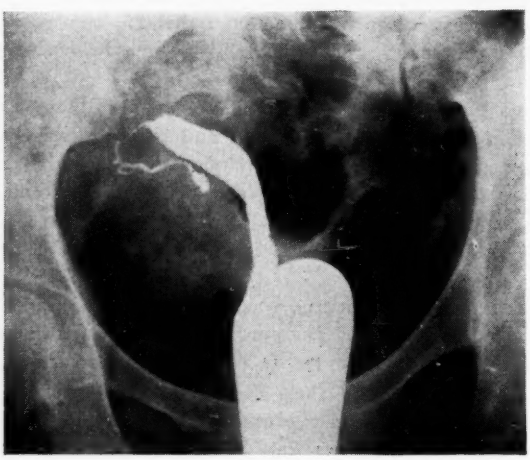

Fig. 2.—Hysterogram two months postoperatively showing a shadow resembling a unicornuate uterus. The tube is patent.

Pathologic examination of the specimen showed that there was a small opening through the pedicle of the horn which communicated with the endometrial cavity of the right uterus. The opened horn showed an endometrium-lined cavity to which the placenta was normally attached. There was a small subserous fibroid on the fundus of the horn.

Except for a mild thrombophlebitis around the transfusion site in the right ankle, the patient made an uneventful recovery. Intravenous pyelography on the tenth postoperative day revealed no anomalies of the urinary tract.

Hysterosalpingograms 2 months postoperatively showed a shadow suggesting an unicornuate uterus on the right, with a single tortuous patent Fallopian tube arising from the tip. No irregularities in contour were present.

Comment

The uterus and vagina are formed embryologically by the fusion of the lower portions of the two Müllerian ducts. Most anomalies which arise in these organs can be explained by lack of fusion in this portion of these structures. Unilateral faulty development following lack of fusion must explain the origin of a rudimentary horn.[1]

A rudimentary horn may end blindly, in which case hematometra and hematosalpinx will occur, following the development of the menstrual cycle. The occurrence of pregnancy in such a structure has serious implications.

There have been only about 100 cases recorded in the literature.[1] Only 9 cases were recorded from 1911 to 1945.[2] The most recent case was reported in 1952.[3] Although the pregnancy can conceivably go to term, the usual termination is by rupture of the defective gravid horn in the fourth or fifth month. When this occurs, catastrophic hemorrhage ensues leading to overwhelming shock, with death occurring within 10 to 15 minutes in 90 per cent of cases.

Diagnosis is usually made at operation or autopsy. There are no absolute methods of diagnosis, and the condition can be recognized only at laparotomy. Other concomitant anomalies such as septate vagina, however, should arouse suspicion. These cases are usually diagnosed as ectopic gestations, and indeed for all practical purposes may be considered to belong to this group of cases. They may be differentiated from tubal gestations by the fact that the round ligament and tube arise lateral to the rudimentary horn.[1]

It is of interest to note that, in 80 per cent of the reported cases, the rudimentary horn did not communicate with the normal horn, and the occurrence of pregnancy must be explained by migration of either the spermatozoon or the fertilized ovum across the peritoneal cavity from the other tube.

Summary and Conclusion

1. A case of pregnancy in the rudimentary horn of a uterus bicornis unicollis with rupture has been presented and discussed.

2. This rare and grave combination cannot usually be recognized prior to operation.

3. Prompt surgical treatment and whole blood transfusion are essential in this condition.

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CASE REPORT OF A RECURRENT ECTOPIC PREGNANCY IN THE STUMP OF A TUBE

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RECURRENT ectopic pregnancy occurs in about 2 to 3 per cent of patients who have previously undergone surgery for an ectopic pregnancy. Recurrent ectopic pregnancy occurring in the stump of a tube which had been left in situ following salpingectomy is, however, very rare.

Falk and Rosenbloom,[1] in 1936, reported a series of 313 cases of ectopic pregnancy. In this group there was only one pregnancy in the stump of the tube following an operation for a similar condition. A careful survey of the literature up to 1953 reveals only forty such cases reported.

Case Report

Mrs. K. F. (No. 255812), a 34-year-old white housewife, mother of four children (aged 13, 11, 6, and 5 years), was admitted to the Elizabeth General Hospital on Sept. 21, 1953.

Her chief complaint was heavy vaginal bleeding which began on September 18. Her menses had been regular, with a cycle of 28 days, lasting four days, normal in amount and painless. Her previous two periods had begun on August 16 and July 18, respectively. The vaginal bleeding at first was painless but on September 20, two days after the onset, the bleeding was accompanied by intermittent lower abdominal cramps with passage of large clots.

On admission to the hospital the patient's general condition was good. On pelvic examination, the cervix felt soft, the uterus was in the anterior position and slightly larger than normal. To the left of the uterus was a rounded, soft mass, somewhat fixed and tender. The vaginal bleeding and cramps gradually lessened and ceased entirely by September 25. The Friedman test for pregnancy was positive. The patient now felt well and at no time did she complain of any pain in the lower left side of the abdomen.

A left uterine pregnancy was suspected, but the past surgical history of this patient complicated the situation somewhat. The appendix had been removed in 1937, and in 1945 she had a ruptured left tubal pregnancy with extensive internal hemorrhage. A salpingectomy was done at that time leaving the cornual stump of the tube in situ. In January of 1947, the patient had been operated upon again for a suspected pregnancy of the stump of the left tube. The operation had revealed an intrauterine pregnancy of six weeks' duration with the sigmoid plastered on the left half of the fundus of the uterus and on the left adnexa. These adhesions were not separated and the abdomen was closed. The pregnancy continued to full term without incident.

In view of this experience and the anatomical-pathological findings present in 1947, it was decided to observe the patient further. On Oct. 10, 1953, the pelvic examination disclosed the cervix and uterus to be about the same as previously, but the mass to the left of the uterus was larger, and the diagnosis of left extrauterine pregnancy became more definite. The second Friedman test was positive and operation was strongly advised.

She was readmitted to the Elizabeth General Hospital on Oct. 13, 1953, with the added history of having had, for the first time, a dull constant ache in the left lower part of the abdomen for the past forty-eight hours. On Oct. 14, 1953, a laparotomy was done. The sigmoid was found to be attached to the fundus of the uterus and to the left mass. All adhesions were separated. The mass, together with the left ovary, was removed en masse by excising the cornual end of the stump of the tube by a wedge resection. The corpus luteum of pregnancy which was in the right ovary was shelled out for microscopic study and the abdomen was closed. The patient made an uneventful recovery and went home on Oct. 21, 1953.

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Gross examination of the specimen showed it to consist of an ovary and an attached portion of tube. The portion of tube measured 5 by 3 cm. On section, the lumen was dilated and contained partially clotted blood throughout which there were numerous fragments of grayish, necrotic-appearing tissue. Microscopic sections of the Fallopian tube showed obliteration of the fimbria and marked thinning of the muscular wall. The lumen contained blood clot within which there were suspended numerous chorionic villi with a double trophoblastic layer. About the periphery there were occasional foci of decidual reaction.

The diagnosis was left Fallopian tube, with ectopic pregnancy; left ovary with follicle cysts; and corpus luteum of pregnancy.

Comment

There are three interesting features of this case. First, the moderately profuse amount of uterine bleeding which the patient had from September 18 to 25; usually with a tubal pregnancy the bleeding is thin, brown-black, and spotting in type. Second, she had two normal intrauterine full-term pregnancies subsequent to the ruptured tubal pregnancy. Third, the pregnancy reported was in the stump of the left tube and the corpus luteum of pregnancy was in the right ovary.

It is conceivable that an ovum might become fertilized in one tube and migrate across the uterine cavity and enter the opposite tube but there is little evidence to support this view.

There is, however, much evidence to support the concept of external migration of the ovum to the opposite side. Kelly[2] reported a case in which he performed a left oophorectomy and a right salpingectomy on a patient, leaving a normal right ovary and a normal left tube. Subsequently, fifteen months later, the patient gave birth to a full-term child; and seventeen months after childbirth the patient was operated on for a ruptured left tubal pregnancy. If the stump of a diseased tube is left in situ, the following may occur: (a) Inflammatory processes may be reactivated in the stump. (b) Adenomyosis may start in the cornual end of the tube. (c) Pregnancy may take place in the stump, as in the case reported.

In order to prevent these possible contingencies, all salpingectomies should be performed by complete removal including a wedge excision of the uterine cornu.

Summary

1. A case is reported of a pregnancy in the stump of a tube which had previously undergone resection for a ruptured tubal pregnancy.

2. The case reported presents strong evidence for "external migration" of the ovum.

3. All salpingectomies should be performed by total excision, including the cornual portion by removing a wedge off the cornu of the uterus.

Acknowledgment is made to Dr. Henry C. Falk for reading the manuscript.

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UTEROPLACENTAL APOPLEXY

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UTEROPLACENTAL apoplexy, the "apoplexie utero-placentaire" of Couvelaire[3] can be classified as an antepartum hemorrhage resulting from the premature separation of the normally implanted placenta. Further consideration of this abnormal state will reveal that not only has the placenta been detached from the uterine wall but also the uterine musculature and sometimes even its contiguous structures have been subjected to profound pathological changes. These changes in all respects have been brought about as the result of an extravasation of blood. Premature separation of a normally implanted placenta was first recognized as such in 1609 by the midwife Louise Bourgeois,[2] the same who attended Marie De Medici through her six labors. In 1776 Rigby[8] differentiated it from placenta previa, in 1901 Holmes[6] suggested the term ablatio placentae. The "apoplexie utero-placentaire" is considered to be a type of ablatio placentae.

The scope of this paper is too limited to attempt much more than a mention of the considered causes for the condition, ranging from emotional disturbances and shortness of the umbilical cord through traumatic influences, endometritis, toxemia of pregnancy, nephritis, histamine intoxication, and torsion of the uterus. Any of these factors may play a part, but none can confidently be looked upon as the primary cause. Desmond[4] in 1857 and Weiss[9] in 1897 each reported a case but neither apparently understood its full significance. In 1911 Couvelaire[3] described one case and in 1912 he described 2 cases. His description, of great significance, associated each case with the clinical findings ascribed to eclampsia. In 1913 Essen-Moeller[5] reported 5 cases and considered them to fall within two categories, namely, those produced by trauma and those resulting from the influence of a toxin associated with eclampsia, eclampsism, and albuminuria. In 1915 Williams[10] reported 2 cases of his own and made a review of the literature with 20 collected cases. In 1919 Ahlstrom[1] reported his 43 collected cases and in April, 1921, Prentiss Willson[12] reported a case of his own and presented for the first time a study of the clinical and pathological data of all cases in the literature to that date. The clinical data so presented covered 69 cases and the pathological data included 46 assembled cases on which observations had been made as the result of either laparotomy or autopsy. Portes[7] collected 73 cases in 1923.

Case Report

R. K., a 23-year-old white primigravida, entered the hospital on Aug. 26, 1952. She was having severe lower abdominal cramps of colicky nature and had been vomiting. The

expected date of confinement was Oct. 16, 1952. She had experienced no serious illnesses nor accidents of any importance, and she had been subjected to no operations with the exception of an appendectomy performed in 1950. The first trimester of pregnancy had been characterized by moderate morning nausea and vomiting but since that time she had felt well. Monthly urinalysis and blood pressure determinations had been normal. On the afternoon before admission she had had some backache which had required her to lie down for relief. She had eaten supper and afterward had felt well and retired at approximately 9:00 P.M. She was awakened at 1:00 A.M. on the day of admission with a rather severe lower abdominal pain and was seen at 1:30 P.M., at which time she was nauseated and vomiting and complaining of steady severe pain. The uterus was firm, hard, and painful to touch. On rectal examination a boggy firmness was felt in the cul-de-sac, but there was no cervical dilatation. No fetal heart sounds could be heard. Her color was good. The blood pressure was 120/70, pulse 100 per minute, and temperature 99° F. She was given 50 mg. of Demerol and sent into the hospital. At 9:00 A.M., Aug. 27, 1952, the pulse was 120 per minute, blood pressure 90/60, and the patient was in pending shock, pale and acutely ill. The chest was clear, the cardiac rate was regular and rapid, and no murmurs were detectable. The abdomen was enlarged in keeping with a 7 months' pregnancy. The uterus was hard and very tender and seemed to be in tonic contraction and was freely movable. There was no bowel distention. No placental souffle was heard. Because of the hardness of the uterus the fetal position could not be determined by abdominal palpation. The extremities were normal. The red cell count was reported as 2.4 million, the white cell count 24,600, and hemoglobin 6 Gm. per 100 ml., with 88 segmented forms, 6 stab forms, and 6 lymphocytes. Blood studies on Aug. 27, 1952, showed a red blood count of 2.45 million, hemoglobin of 6.7 Gm., and hemocrit 22 volumes per cent. The prothrombin time was 21 seconds compared with a control of 25 seconds. A red blood fragility test was normal and a study of the stained smear showed no evidence of blood dyscrasia.[13] Repeated prothrombin activity tests during the first five days of hospitalization were normal. Blood typing and cross-matching were carried out, and the patient proved to be type 0, Rh negative. She was prepared for surgery with a preoperative diagnosis of ablatio placentae with concealed hemorrhage.

At operation through a low midline incision, it was noted that throughout the entire uterus, both ovaries, and for some extent into the broad ligaments there was gray-black discoloration due to subperitoneal and intramural hemorrhage. There was about 300 c.c. of bloody fluid in the cul-de-sac, and the uterus was enlarged to approximately eight months' gestation. Supracervical hysterectomy was performed; and the right ovary was then removed. The uterus was opened, and no bleeding was found in the amniotic sac; some large clots were present in the uterine cavity.

The tissue report was as follows: *Gross:* The specimen consisted of a uterus containing placenta and fetus. The uterus measured 28 by 15 by 12 cm. The serosa had a mottled gray-blue purple color. Within the cavity of the uterus there was a male fetus measuring 15 cm. in length. The placenta was separated almost entirely from the uterine wall by a mass of clotted blood. The entire wall of the uterus had been infiltrated with blood and had a bluish-purple color. There was also an ovary which had a bluish-purple color and was firm. It measured 4.5 by 3 by 2 cm. On sectioning it was purplish and meaty. *Microscopic:* In many areas the muscle bundles of the myometrium were separated by extravasations of blood. The better-preserved muscle fibers were swollen and took a pale pink stain. At the placental site a decidual reaction was seen. The ovary showed many areas of extravasation of blood. Between these areas well-preserved ovarian parenchyma was present.

Diagnosis: Apoplexy uteri (Couvelaire uterus).

The hospital course was uneventful and the patient was discharged on the sixth day. She received 1,500 c.c. of whole blood during and following surgery and received an additional 500 c.c. of whole blood on the third hospital day.

Since uteroplacental apoplexy can be definitely diagnosed ante mortem only by means of laparotomy, the decision must be made, whether, after cesarean section, should the uterus be allowed to remain or be removed, or whether abdominal hysterectomy without opening the uterus should be carried out. It is evident that the extent of involvement determines the decision. In some series the abdominal hysterectomy without opening the uterus carries a maternal mortality of 50 per cent, the Porro section carries a mortality of 47.6 per cent, and cesarean section carries a maternal mortality of 19 per cent.[11, 12] It seems from the cases collected by Willson that the prime factor in the decision for Porro section was based upon the extent of the lesion. Likewise, it seems that those patients subjected to the Porro type of operation had a concomitantly more severe type of toxemia. Another item of primary importance appears to be the time factor between the onset of symptoms and the eventual termination of the case.

Summary

1. A review of the literature reveals, we believe, that the most tenable explanation for uteroplacental apoplexy is that it results from a toxin (a fibrinolysin) which possesses hemorrhagic properties producing thrombosis and endotheliolysis and inhibiting blood coagulation by a reduction in fibrinogen concentration and a reduction in prothrombin activity. The toxin demonstrates itself first locally and second systemically.

2. A case of uteroplacental apoplexy is reported. There was no evidence of a generalized distribution of a hemorrhagic toxin, the only evidence of the presence of such toxin being confined to the uterus and its contiguous structures.

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HYDATIDIFORM MOLE IN A 53-YEAR-OLD PATIENT

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THE recent report of Gaetane and Labriola[1] of hydatidiform mole in a 54-year-old patient, in which they emphasized the parity of the disease at this age, prompted this report.

Case Report

A white woman, No. 50-1219, aged 53 years, first came to the Grand Forks Clinic on Feb. 8, 1952. She complained of anorexia, nausea and vomiting, and pain in the lower abdomen of three weeks' duration. These symptoms were gradual in onset and never severe. There were no sharp pains at any time and there was no vaginal bleeding. She believed she had lost some weight. Bowel movements were regular and there were no urinary tract symptoms.

Menstruation was normal until 1951 when there was minor irregularity. No dysmenorrhea, leukorrhea, or intermenstrual bleeding had been noted. Her last menstrual period occurred during the last week of November, 1951.

She had had five previous deliveries without complications. Her last child was born in 1940. Family history: Her father died of a malignant tumor of the leg, type undetermined. Her mother died of diabetes mellitus and one brother died of heart disease.

On March 28, 1951, I did a curettage, trachelorrhaphy, and anterior and posterior colporrhaphy upon her. Microscopic section of the tissue removed revealed a proliferative endometrium, no cervical carcinoma, and a benign cervical polyp.

Examination on Feb. 8, 1952, revealed the following: blood pressure of 160/90, a soft systolic murmur at the apex, a questionable mass, felt on deep pressure, in the left lower quadrant of the abdomen. Pelvic examination revealed a multiparous introitus, normal external genitals, a soft, clean cervix and well-supported anterior and posterior vaginal walls. The uterus was soft, irregular in outline, in anterior position, and enlarged to the size of an eight weeks' gestation. The adnexal areas were normal. These findings were confirmed by rectovaginal examination. The impression was of a possible uterine myoma and early intrauterine pregnancy. She was given symptomatic treatment and told to return in two weeks.

The patient's husband called on Feb. 13, 1952, to report that his wife's condition was much worse. Anorexia, persistent nausea and vomiting were alarming. Insomnia was troublesome and the patient's fear of pregnancy was so great that she had threatened suicide. She was hospitalized. There had been a weight loss from 168½ pounds to 164½ pounds in the intervening five days. The temperature was 99.2° F., pulse 80, and blood pressure 160/100 on admission. Except for moderate dehydration and some increase in the softness and tenderness of the uterus, there had been no essential change in her physical condition since the initial examination. Our impression was that she had severe nausea and vomiting and an early intrauterine pregnancy. A Friedman test was reported positive on Feb. 20, 1952.

Following medical and obstetric consultations, a total abdominal hysterectomy with bilateral salpingo-oophorectomy was done on Feb. 22, 1952. A photograph was taken of the incised uterus (Fig. 1) which shows the gross pathology rather clearly.

Her postoperative course was uneventful and she was discharged from the Deaconess Hospital on March 7, 1952. An x-ray examination of the patient's chest while she was in the hospital was negative for any areas of increased density.

The report by J. S. McCartney, Department of Pathology, University of Minnesota, was as follows: "The whole uterus is 11 by 8 by 6 cm. There is a mucus plug in the cervix. The cavity of the uterus is occupied by what is apparently amniotic sac about 7 cm. in diameter, and placental tissue. There is a separate mass of material which looks like placenta. It is 6 by 5 by 2 cm. and contains cystic villi up to 0.5 cm. in diameter. The left ovary is 3 by 2 by 1 cm. and its tube is 6.5 cm. in length. The right ovary is 2.5 by 2 by 1 cm. and its tube is 6.5 cm. in length. Sections from the body of the uterus show hyperplastic glands and decidual reaction. Another area shows masses of trophoblast and decidua and a degree of adenomyosis. The third section of the body of the uterus shows also hydropic villi and areas of necrosis. There are no evidences that I can see of a chorionepithelioma. The section of the separate mass shows the characteristic appearances of hydatidiform mole."

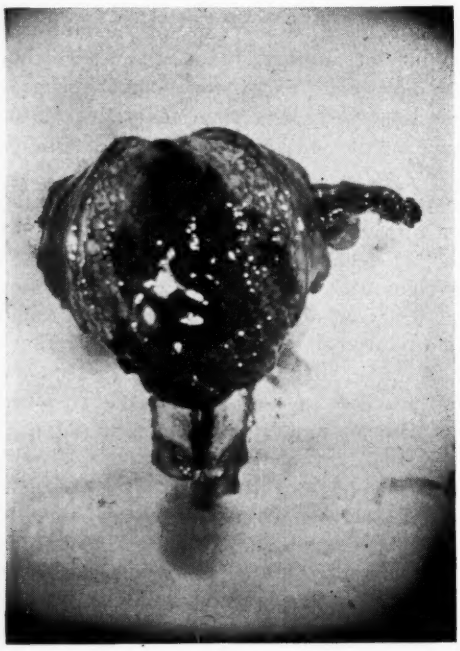

Fig. 1.—Mole projecting through the widely incised uterus.

Friedman tests on March 7, 1952, and on April 9, 1952, were negative. I asked Dr. McCartney to send representative specimens of this tumor to Dr. Emil Novak for inclusion in the Chorionepithelioma Registry. In personal communications to Dr. McCartney and to me, Dr. Novak[2] reported, in part, as follows: "These slides represent what I would interpret as a benign hydatidiform mole with no histologic suspicion of chorionepithelioma. Rather large fields of decidua are seen, with considerable trophoblastic infiltration (syncytial deciduitis) in addition to the actual hydatidiform villi, which show a moderate amount of trophoblastic proliferation. There is, however, no histologic suggestion of malignancy, and since a hysterectomy was done I do not believe that you need be concerned about the prognosis. Incidentally, and with of course, no relation to the mole, one of the ovaries shows a cluster of the so-called hilus cells which are looked upon as the ovarian homologues of the Leydig cells."

At her last examination, Nov. 25, 1953, the patient's blood pressure was 138/80, and vaginal examination was negative. An x-ray of the chest was negative. The urine was negative. Blood examination showed the following: hematocrit, 43 per cent; erythrocytes, 4.55 million; leukocytes 9,700 with a normal differential count and a sedimentation rate of 20 mm. in one hour (Westergren).

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A MODIFIED MYOMA SCREW AND UTERUS HOLDER

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THE metal screw with a transverse bar or a loop as a handle has been standard instrument equipment in most gynecologic operating rooms for many years. It afforded a means whereby solid benign tumors, usually myomas, could be elevated in order to give exposure and expedite removal. Attempts to accomplish this by traction on a conveniently located, pedunculated myoma were usually fraught with tearing and excessive bleeding; altogether too frequently the usual type of myoma screw caused the same complications.

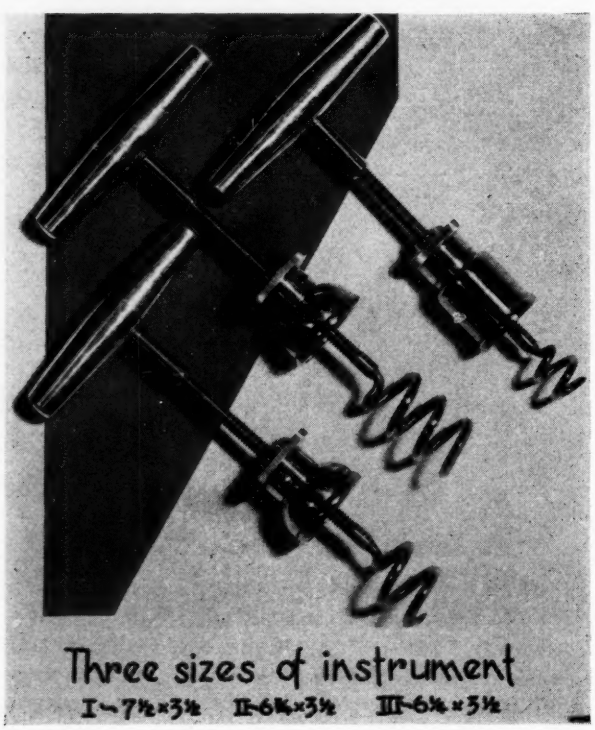

Fig. 1.

The central areas of myomas are relatively avascular, but the arteries and veins over the outer surface areas are enlarged and tortuous with frequent varicosities. Puncturing or twisting and tearing across these peripheral areas resulted in sufficient blood loss to obscure visibility and necessitated speedy identification and clamping of the major blood supply.

Myoma screws (Fig. 1) were devised with an adjustable cup between the turns and the handle. After insertion of the screw the cup can be turned down firmly and secured, thus providing a tamponade of the vascular area and preventing surface movement and tearing (Fig. 2). Two sizes are used for the large and medium-sized myomas, respectively, and a third type is for use on a normal-sized or slightly enlarged uterus and for myomectomy. This third type has a shorter diameter and length of the screw as well as a deeper cup for the more compressible tissue. More than one of these screws* could be used in a single group of pelvic tumors.

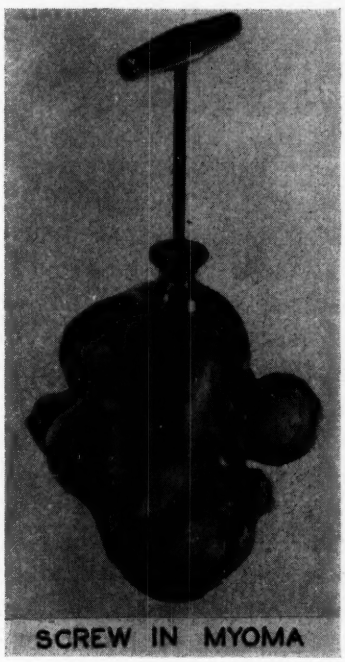

Fig. 2.

These instruments are much less traumatic to the removed specimen than sutures or the various vulsellum forceps. Actually the pathologist might have difficulty identifying the screw puncture site. They should not be used when there has been histologic proof or there is clinical suspicion of malignancy. It would be inadvisable to insert them into tissue not subsequently removed.

*Further information on these instruments may be obtained from Wedler Brothers, Inc., 1535 E. 38th Street, Cleveland, Ohio.

Editorials

The International Congress of Gynecology and Obstetrics

The International Congress of Gynecology and Obstetrics was held at Geneva, Switzerland, from July 26 to July 31, 1954. This meeting was in a sense the lineal descendent of other International Congresses held before World War I and to some extent the successor of the Congress held in New York City in the spring of 1950. The Geneva Congress was a notable success in many respects.

The total registrations for the Congress numbered 1,822. The group from the United States was the largest with 457 participants, followed by Germany with 210, Switzerland with 200, and France with 167. It was interesting to note that, although the numbers were small, delegates were present from Poland, Russia, Czechoslovakia, and Hungary. Another interesting feature was the apparent lack of interest in the Congress in Great Britain, since only 27 persons registered from that country. Altogether, 54 countries situated in all parts of the world were represented.

The scientific aspects of the program were classified as "official reports," of which there were 89 in gynecology and 80 in obstetrics, and as "free communications," of which there were 78 in gynecology and 69 in obstetrics. In order to provide space for these 316 presentations, the Congress met concurrently in five separate assembly halls. As a result of this necessary subdivision, the attendance at times seemed rather small, but this was perhaps only the inevitable result of providing forums for so many who wished to speak. In each hall, simultaneous translation was available into French or English.

A feature indicating the pains expended in the preparation of the Congress was the availability to all registering at the beginning of the Congress of a printed and bound copy of all scientific contributions. An occasional comment was heard that this made it unnecessary to attend the actual sessions and so perhaps reduced attendance slightly, but this disadvantage seemed hardly comparable with that of the delay usually occurring before the appearance of such transactions.

Prior to the opening of the Congress, much work had been done by a special committee in drawing up a form of Constitution for an International Federation of Gynecology and Obstetrics. The national societies of the various countries had been asked to review the proposed Constitution and to send delegates with authority to approve or modify the provisional document. The American delegation consisted of representatives sent by the American Gynecological Society, the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, the American Academy of Obstetrics and Gynecology, the American Committee on Maternal Welfare, and the Section on Obstetrics and Gynecology of the American Medical Association.

The Constitution was read section by section, criticized, and approved by the delegates sitting in a large hall, each supplied with earphones giving necessary translations. At times, the procedure seemed a miniature, even a parody, of a United Nations Assembly, and politics appeared to hover over the scientific attainment of common objectives. Eventually, however, and with a minimum of tension, a Constitution was approved.

An Executive Board of the International Federation was elected with the following Officers:

President:	Professor H. de Watteville (Switzerland)
Vice Presidents:	Professor L. Gérin-Lajoie (Canada)
	Professor E. Cove (Italy)
Treasurer:	F. L. Adair, M.D. (U. S. A.)
Secretary:	Professor R. Keller (France)

Additional members of the Executive Board were designated from Argentina, Brazil, Germany, Great Britain, India, Japan, Mexico, New Zealand, Russia, and the United States. Dr. W. Geisendorf of Switzerland was elected Executive Secretary, and Geneva designated as the site of the permanent office.

It was decided that the next Congress should be held in the year 1958 in Montreal.

Altogether, it appeared that in the International Federation a new medium for the exchange of medical knowledge had been founded, and that a beginning had been made of an institution which might contribute significantly to the possibilities of international contact and friendship.

H. C. T.

Misappropriation of Patients

Much has been said and written about the evils of fee splitting, which even the participating culprits must recognize as a reprehensible practice, but little or nothing has been offered constructively to minimize some of the fundamental factors which have contributed to the growth of this commercialization and prostitution of an honorable profession. Two of the most important of these are the either thoughtless or deliberate unwarranted retention of other physicians' patients by surgical specialists, and the failure of some specialists for selfish reasons to refer their own patients to other physicians better qualified to diagnose and treat the immediate complaint. He who is expert in one field of medicine should limit his work to his chosen sphere and shun comparative mediocrity in another arena.

Surgical specialists should never forget that a patient acquired from another doctor should remain in his charge thereafter and should be sent back to him just as soon as the patient's condition permits, and the specialists must not accept the same patient on any future occasion without a repeated referral from the original source, regardless of the number of intervening months or years. This of course has no reference to the right of all patients to change their

personal physicians at their own volition. Neither are patients to be operated on nor otherwise treated when sent for an opinion only, without a subsequent definite request for such procedures. When it seems desirable that a referred patient be surveyed by someone else in a third field of practice, the referring physician should be so advised and asked to make the selection. Universal strict adherence to these ethical principles will so augment the practice and increase the professional income of others, particularly general practitioners and internists, that the demand for split surgical fees will automatically diminish.

Too many surgeons tend to continue the patient's postoperative treatment after the hospital discharge, when the wound dressings, the correction of anemia and avitaminosis, and other nonsurgical details can be equally as well undertaken by his or her own physician. Others are not too conscientious about their acceptance of a patient previously operated on when some entirely new symptom complex develops at a later date. Under such circumstances the surgeon should politely but firmly suggest that the patient must see the family doctor first. Surgical specialists have been known occasionally to make excursions into foreign fields, and assume the responsibility for the treatment of diabetes, rheumatism, hypertension, and many other purely medical conditions in affluent patients, rather than to refer them elsewhere. All of these offenses tend to aggrandize the surgical specialist at the expense of the medical man and keep the patients who properly belong there out of his office. If the surgical specialists would present a united front of professional and ethical fairness, and do everything possible to enhance the prestige and build up the practice of the general practitioner and internist, the financial hunger of the latter group would be materially reduced and the demand for fee splitting incidentally lessened.

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Review of New Books*

Erythroblastosis Fetalis, Report of the Seventh M. & R. Pediatric Research Conference, 1954, M. & R. Laboratories, Columbus, Ohio. 78 pages, 22 figures.

This report covers the symposium on erythroblastosis fetalis and kernicterus held at Children's Medical Center, Boston, Nov. 21 and 22, 1952.

The purpose of the conference was to assist in the correlation of the latest information on specific topics of general interest in the practice of pediatrics, and to stimulate further research by the exchange of such information.

The report is divided into five chapters, each dealing with a major problem in erythroblastosis. A round table presentation is carried out in each chapter by a panel of outstanding clinical and research workers in the field. The latest ideas and theories together with a synopsis of the most recent animal and histopathological studies are presented.

The treatment of erythroblastosis is adequately covered, along with a discussion of the hazards of exchange transfusions and the handling of these emergencies should they arise.

The final chapter is a detailed description of the technique of exchange transfusion used at the Children's Hospital, Boston, and at several of the other teaching hospitals in this area. It will be of great help to any hospital in which an exchange transfusion technique is being standardized.

No attempt was made to cover the whole subject in this report. It is presented rather as an interchange of ideas on the most troublesome problems in erythroblastosis.

Proceedings of the Society for the Study of Fertility, No. 5, Liverpool Conference, Cambridge, England, 1953, W. Heffer and Sons. 105 pages. $1.40.

This book contains the proceedings of a conference sponsored by the British Society for the Study of Fertility. Sixteen articles were presented, ten of which are clinical studies and six are concerned with laboratory animal investigations relating to infertility. Of particular interest is the paper by T. N. A. Jeffcoate, who analyzed 1,023 consecutive tubal patency tests to evaluate their reliability. He noted that 43 of 116 negative insufflation tests and 13 of 86 salpingograms were erroneous. Even when both of these examinations gave negative results, pregnancy occasionally followed. Jeffcoate is of the opinion that the character of tubal oscillations is of little value in diagnosing tubal development or disease, other than occlusion.

Another presentation of interest is the one by B. Sandler concerning the mechanism of tubal spasm. He postulated the presence of a functional sphincter at the uterotubal junction and suggested the possibility of an arteriovenous anastomosis in that region. The effects on testicular function and spermatogenesis in laboratory animals are analyzed subsequent to the following surgical procedures: (1) interruption of the arterial flow to one testicle; (2) ligation of the seminal vesicles; (3) ligation of the vasa efferentia; and (4)

*The Advisory Committee on Policy has agreed that most book reviews need not be signed.

unilateral orchidectomy. Correlations were made with similar clinical lesions. Other papers of interest are one by A. S. Parkes on "The Quest for the Ideal Contraceptive," and by G. I. M. Swyer on "The Effects of Testosterone Implants in Men With Defective Spermatogenesis."

Those who are concerned with the problems of fertility and sterility would benefit from reading this volume.

Hypertension and Nephritis. By Arthur M. Fishberg. Fifth edition. 986 pages with 49 illustrations. Philadelphia, 1954, Lea & Febiger. $12.50.

The middle-aged and younger generations were brought up on earlier editions of this book. Reading the new edition is something like recapturing "the good old days." As frequently happens, the satisfaction of nostalgia is disappointing.

The last chapter of the book, dealing with the toxemias of pregnancy, were better omitted. A partial list of statements unacceptable to the reviewer follows: The fetal mortality in pregnancies complicated by glomerulonephritis is 47 per cent. Pregnancy has a "decidedly adverse" effect upon the disease, which may continue even after termination of the pregnancy. Pregnancy increases the excretory work of the kidney. Renal disease is "the most common cause of *abruptio placentae*." Peters' report that pyelonephritis underlies a high proportion of the toxemias is quoted without mention of the several negative reports which shortly followed.

It may be that "a high proportion (majority) of the pregnant women in whom elevated blood pressure is found are suffering from essential hypertension," but it seems doubtful that "in most of the cases this is proved immediately by the finding of hypertension . . . early in pregnancy." Two papers are cited on the course of pregnancy in women with essential hypertension: one is nearly 30 years old and the other (erroneously keyed in the text) is perhaps the poorest ever published on the subject. Fishberg advises against pregnancy if the blood pressure be 150/100 or more and recommends therapeutic abortion if "a blood pressure of up to about 170/110 mm. be found early in pregnancy without any symptoms."

In fatal eclampsia, cerebral hemorrhage certainly is found in more than "rare cases." It is not true that eclampsia "occurs only in the presence of marked hypertension." Nor is it "rare for hypertension and proteinuria to make their appearance . . . without antecedent abnormal weight gain."

The data for perinatal mortality in the various toxemias are cited from a paper published more than 20 years ago. The author thinks it very probable that the incidence of residual hypertension bears some proportion to the duration of toxemia, "although I know of no detailed statistical proof." The relation has been established in a score of papers.

The other chapters of the book are uneven. Some are very good, others not. The first chapter, dealing with the physiology of the kidney, falls between two stools. It will be difficult to understand for one not conversant with renal physiology, but superficial and garbled for one who is.

While there is a long chapter on the necrotizing nephroses, one has to hunt through the book for the management of such cases. A system can be synthesized from isolated statements scattered through several chapters.

By and large, the book organizes a tremendous amount of information. Many sections begin with succinct historical reviews and end with extensive lists of references. The book is well made physically except for an undue number of typographic errors.

Children for the Childless. Edited by Morris Fishbein. 214 pages. Garden City, N. Y., 1954, Doubleday & Company, Inc. $2.95.

From the scientific point of view, this book is well written and authoritative. It is comprised of eight chapters each written succinctly by men who have a background of

experience and depth of understanding of the problems facing childless couples. Although the first chapter, "On Being a Parent Today," and the last one, "What Will Our Child Be Like," are enlightening, they do not contribute to an explanation of sterility. The chapter by Dr. Eastman on "Human Fertility" is a well-documented population study and has crucial social implications. It does not, however, aid or comfort childless couples interested in procreation. Excellent discussions of the physical and psychosomatic aspects of fertility and sterility should enable many lay people to comprehend better and adjust to the problems of early marriage and fertility. Dr. Rubin's discussion of "Human Sterility" is a fine analysis of the problem. Many couples have gone through life childless due more to a lack of knowledge than to a specific organic disturbance. Dr. Rubin's discussion leaves the reader who has a specific problem with a clear mind and a release from the tension and fears of fertility investigations. The subjects of artificial insemination and adoption are presented well and will clarify many misconceptions ascribed to both procedures.

The book is to be recommended to couples who seek an accurate and clear presentation of diagnostic and therapeutic methods in infertility.

Die Viruskrankheiten in der Gynäkologie und Geburtshilfe. By Meta Sander, University Woman's Clinic. 137 pages. Leipzig, 1953, Georg Thieme. DM 9.60.

This monograph is a concise series of descriptions of all the virus diseases of man, and some of those of animals. Each disease receives two or three pages of historical and clinical discussion, and each section is followed by a short bibliography. Finally twenty pages are devoted to a consideration of the relationship of virus diseases to the genitals and to childbearing.

It is pointed out that the virus diseases pertain principally to childhood and early adulthood. This is because they confer a strong and lasting immunity. By and large, the male sex shows a greater morbidity in relation to virus diseases. There is no purely gonadotropic virus. The author concludes that virus diseases are influenced by hormonal factors far more than by any other physiologic event.

This little book may serve as a convenient reference, since it embodies much information not readily available without extensive reading.

Resuscitation of the Newborn. By Joseph D. Russ. 55 pages. Springfield, Ill., 1953, Charles C Thomas. $2.50.

This small book in the Thomas Lectures series deals with asphyxia in the newborn and its definitive and prophylactic treatment.

Apparently the book is a collection of lectures to either medical students or nurses. The presentation is markedly oversimplified and does not seem very thoughtful. The author recites several concepts which might be surprising to obstetricians. For example, on page 15, the following appears, "The existence of an anemia in the mother produces a corresponding relative anemia in the infant." On the very next page the reader is told, "The existence of such pathology (kidney disease) is quite often aggravated by pregnancy with mild toxic products present in the blood stream. These are passed on to the baby with resultant generalized toxicity."

The circulation of fetal and maternal bloods through the placenta is changed from our usual concepts, when on page 28 we are told, "*Bleeding placenta previa or abruptio placentae:* The blood loss in the fetus, in either condition, may be sufficient to cause moderate to severe asphyxia."

The last such concept to be recorded in this review also is found on page 28. It appears as follows, "Babies born of toxic mothers (toxemias of pregnancy) present signs and symptoms similar to those found in the mother."

There is an extensive bibliography of 139 references.

Gynecological and Obstetrical Anatomy and Functional Histology. By C. F. V. Smout and F. Jacoby. Third edition. 336 pages with 186 illustrations. Williams & Wilkins Company. $7.00.

This readable and concise book affords a complete survey of anatomy, histology, embryology, and endocrinology as they apply to the field of obstetrics and gynecology. The authors have done a remarkable job in covering so much ground in such short space without sacrificing clarity.

The anatomical sections are excellent and include a discussion of prolapse. The endocrinology is concisely yet clearly presented in a very readable fashion.

The book is certainly worth while and should interest both student and specialist.

A Textbook of Gynaecology. By K. M. Mansani. 639 pages with 261 illustrations. Bombay, India, 1954, The Popular Book Depot. Rs 17/8.

In an attempt to present a rather vast subject matter, this volume is severely handicapped not only by the limitation in space but also by poor illustrations and composition. The author has scratched only the surface in the sections devoted to endocrinology, sterility, psychosomatic disturbances, and modern adjuncts of surgical care.

While perusing the chapter on fibromyomas, this reviewer was surprised to read: "a subtotal hysterectomy is preferable to a total hysterectomy when the cervix is healthy and there are multiple growths situated in the body of the uterus above the level of the internal os." Later in the presentation of various operative procedures, the author unhesitatingly states that the indications for total hysterectomy are only in the case of: "cervical fibromyoma and when the cervix is either elongated or badly lacerated." Inasmuch as this advocacy of the subtotal hysterectomy is so contrary to customary principles of therapy in the United States and elsewhere, one wonders if this concept represents merely a personal expression of Dr. K. M. Mansani or a widely accepted program in India.

In recent years, there has been a great deal of research and progress in the various branches of gynecology. This work represents an important part of the specialty and should be included in any complete textbook of gynecology. Although the author has adequately covered many of the aspects of the subject matter, the volume is for the most part sketchy and disappointing.

El Cancer Ginecologica. By Jual Carlos Ahumada, Professor Titulor De Clinica Ginecologica en la Universidad de Buenos Aires. Two volumes, 1018 pages with 634 illustrations. Buenos Aires, 1953, "El Ateneo."

Many books have been written on the subject of gynecological cancer but certainly none more comprehensive than *El Cancer Ginecologica.* The fields of cancer of the vulva, vagina, cervix, corpus, and ovary are amply covered in all respects. In addition, there are complete sections devoted to mammary malignancies, choriocarcinomas, sarcomas, and roentgen therapy. The gross and microscopic pathology is beautifully illustrated with both colored and black and white plates. Similarly the operative procedures are very well portrayed.

Another unique feature of these volumes is the rather extensive bibliography which should be a valuable reference source for future investigators and clinicians in the field of cancer. Professor Ahumada and his collaborators are to be commended for their thorough compilation and interesting presentation. Their work represents a significant contribution in the field of medical literature.

A la Recherche d'une ethique médicale. By Louis Portes, President du Conseil National de l'Ordre des Médecins. 210 pages. Paris, 1954, Presses Universitaines de France.

This is an extremely interesting volume edited by Masson et Cie of France. It deals with many of the current problems in medical ethics and discusses their philosophical and traditional background. In addition to a review of such items as euthanasia and the medical secret, there is a substantial portion of this text devoted to obstetrical ethics.

Causes of Prematurity: A Clinical Investigation. By Svend Nørregaard. 240 pages. Copenhagen, 1953, Arne Frost-Hansens Forlag.

This sizable monograph is the doctoral dissertation of a candidate for the M.D. degree of the University of Copenhagen. A very large amount of factual material on the etiology of prematurity is set forth in an orderly and scholarly manner. The author points out that infant mortality in most civilized countries has decreased considerably during the twentieth century, whereas mortality during the first month of life and the incidence of stillbirths have declined only slightly. As a result, neonatal mortality has come to play an increasingly important role in infant mortality. Causes of neonatal deaths during the first month of life are chiefly the so-called congenital diseases, but these diseases only rarely lead to death after the first month. The author discusses the possibility of reducing mortality due to these congenital causes, and concludes that, even though a certain reduction is possible, it will hardly be very significant as regards most of these congenital diseases apart from prematurity.

In his second chapter, the author gives an extensive and detailed account of the incidence of premature births, and concludes that any hope of further reducing infant mortality depends on lowering the mortality due to premature birth. A detailed account is then given of the author's specially studied material. This comprises 1,030 premature deliveries, constituting 6.5 per cent of all births in Copenhagen during 1948. In this group there were 1,125 premature infants, constituting 7 per cent of all newborn infants for that period. Twenty per cent of the children in this series were twins, whereas in the control series comprising 1,000 deliveries, only 0.5 per cent were twin births. Careful biometric analyses of these premature infants are presented. One of the conclusions drawn is that the weight distribution among premature children in whom constitutional factors of one sort or another are present differs from that found among other premature children in that the average weight is greater and the period of gestation is generally longer in infants whose family history indicates predisposition to prematurity in the mother's family. Attempt is then made to correlate the social conditions of the mothers in the series studied with those in the control series. There was found to be a rather pronounced difference between these two series as far as the lowest weight groups are concerned.

Maternal morbidity in the two groups is analyzed. The incidence of syphilis among the mothers was somewhat higher in the premature series than in the control series, regardless of social status. The author believes that there is no doubt as to the qualitative significance of syphilis, though quantitatively this condition no longer constitutes a major problem. The mothers in the premature series had a higher incidence of albuminuria during pregnancy, as well as more hypertension and visual disturbances; the incidence of edema, on the other hand, was higher among mothers in the control series. The incidence of early as well as late vaginal bleeding was far greater in the premature series than in the control series. Mothers in the premature group had a somewhat greater incidence of cardiac disease, but the author concludes from his data that these disorders can give rise to premature delivery only in those cases where cardiac insufficiency develops during pregnancy itself. Diseases of the respiratory tract occurred more frequently in the premature series than did infections in general. Furthermore, mothers with fever at the onset of labor produced stillborn offspring with markedly increased frequency in the premature series.

These are representative topics dealt with in this exhaustive survey of the subject. There is an extensive bibliography, and the author has spared no pains to make his monograph extremely comprehensive. He shows rather conclusively that the prevention of prematurity depends to a considerable extent on adequate prenatal treatment and care. One can only admire the industry and carefulness which are evident on every page of this consequential dissertation.

La Sterility Coniugale (Conjugal Sterility). By Beniamino Sorrentino and Michelangelo Sorrentino. 282 pages with 32 illustrations. Rome, 1954, Abruzzini Editore.

The Professors Sorrentino, respectively an obstetrician-gynecologist and a urologist, have collaborated in this recent Italian work on sterility and infertility in which approxi-

mately equal space is devoted to the viewpoint of each of the two disciplines. Most of the following commentary refers to the first section, which deals with infertility in women.

The opinions of Prof. Beniamino Sorrentino on female infertility differ so markedly both in principles and in detail from commonly accepted theory and practice in the United States that objective evaluation of his section of this work is difficult. The introductory section on basic embryology with which the work begins is characterized by a perhaps intentional oversimplification of the basic fundamentals; even so, it completely omits such fundamental features as the theca cone of Strassman, and the recent work on fertilization of Shettles and others. In the section on voluntary sterility the work discards all semblance of a scientific treatise, and becomes a frank anticontraceptional polemic. The practice of coitus interruptus is attacked as being a frequent etiological factor in cardiovascular disturbances and gastrointestinal upsets as well as symptomatic ovarian cysts and uterine myomas. Disastrous cases culled from the literature to illustrate the deleterious effects of chemical and mechanical methods of contraception are condemned on the basis of these specific instances. The teachings of the Catholic Church on various types of contraceptive practices are treated with full scholastic argumentation.

Sorrentino states without citing evidence that orgasm in the female definitely facilitates impregnation, and that the time of sperm migration is always longer if the woman has not had orgasm. Orgasm in women is interpreted as a physiologic, not as a psychic, phenomenon. In his discussion of the histology of the endometrium at various phases of the cycle, Sorrentino presents the classic factual data, but entirely ignores the important work of Bertil Falconer on the interpretation of subnuclear vacuolization. He maintains that 34 per cent of all his patients with primary sterility have a specific syndrome consisting of genital hypoplasia without other stigmas. He further believes that many pubertal menstrual dysfunctions can be traced to congenital syphilis, and that this disease often presents sterility as its only symptom. In a detailed discussion of tests for ovulation, Farris's test is not mentioned. Rules of thumb for the administration of gonadotrophic hormone preparations are given in considerable detail, but there is virtually no discussion of indications and contraindications for their use. Many American gynecologists will fail to share Sorrentino's apparently enthusiastic recommendation of procaine infiltration of the cervical sympathetic ganglion as the best method of producing ovulation in patients with anovulatory cycles. Electroshock therapy is suggested as acceptable treatment for obscure menstrual dysfunctions. The injection of lyophilized placental extract seems a rather startling treatment for acute exacerbation of pelvic inflammatory disease. Hysteropexy and ovariopexy are uncritically recommended for sterile patients with uterine retrodisplacement. Sorrentino emphatically states that salpingitis isthmica nodosa is always due to endometriosis, never to salpingitis. Endometrial endosalpingeal polyps are stated to be the lesion responsible for sterility associated with endometriosis. Strange also is the author's statement that status thymicolymphaticus is characteristically associated with genital hypoplasia, ovarian fibrosis wih follicular destruction, and menstrual aberrations, and may be diagnosed when these findings coexist.

The author discusses effects of chronic alcoholism and the use of tobacco on fertility at the level of a frank polemic. It is his opinion that chronic toxic ovarian damage is a constant sequel of the use of alcohol and tobacco, and that women are much more susceptible than men to damage from nicotine, which brings about a delayed menarche and assorted menstrual aberrations. About 75 per cent of women who smoke heavily are said to exhibit genital dysfunction of some type as the direct effect of their smoking habits. This section ends with vigorous expression of the author's opinion that intensive propaganda campaigns designed to convince women of the dangers of smoking and drinking would be of enormous value as a prophylaxis against infertility and sterility.

The therapeutic value of uterotubal insufflation and hysterosalpingography is emphasized at the expense of their diagnostic value. Although most of the book does not deal with surgical techniques, various methods of performing salpingostomy and ovarian uterine implants are illustrated by a series of mediocre drawings.

As this résumé indicates, this volume cannot be recommended as a competent modern book on its subject. The author's viewpoints are empiric and narrowly doctrinaire. Dogmatic statement routinely replaces the judicious weighing of scientific evidence, and a superficially exhaustive listing of miscellaneous "data" produces a fallacious illusion of thoroughness, especially when it is realized that many recent researches of commonly conceded scientific merit have been completely ignored.

The section on sterility in the male by Professor Michelangelo Sorrentino, although in many ways considerably more judiciously presented than that of Professor Beniamino Sorrentino, shows many similarities of approach. The long bibliography at the end of the book, though of impressive bulk, is composed largely of Italian and French sources, and would have only very limited usefulness for the physician interested in an exhaustive bibliography on this subject.

It should be added that the book is printed on a very good quality of leaded paper, and that the often mediocre illustrations are well reproduced. The print is legible; the proofreading has been carefully done; and the binding (unlike the contents) is serviceable and sturdy.

Congenital Heart Disease. By Henry S. Kaplan and Saul Joel Robinson. 126 pages with 146 illustrations. New York, 1954, McGraw-Hill Book Company, Inc. $12.50.

While this book is not directly concerned with obstetrics and gynecology, it is thought worth while to bring it to the attention of specialists in this field because of the frequency with which congenital heart disease is met in the newborn. This is a small, 126 page atlas, profusely illustrated, setting forth some of the principles of differential diagnosis; the major electrocardiographic changes and the radiologic features of each congenital abnormality. Each x-ray is reproduced in duplicate and superimposed upon one of them is a drawing of the heart giving the relative position of the great vessels and chambers. The technique is extremely effective.

This book does not pretend to be a definitive work on this subject, but is merely meant as an introduction and a guide to the general practitioner and those not particularly concerned with the field. It certainly does not compare in scope with Dr. Taussig's "Congenital Malformations of the Heart," nor does it attain the stature of the great atlas by Dr. Maude Abbott. It is a useful text, however, pleasingly and well presented.

Standard Values in Nutrition and Metabolism. Edited by Errett C. Albritton. 380 pages. 1953, Wright Air Development Center, Ohio.

This second part of a *Handbook of Biological Data* is a compilation of 160 tables covering many phases of nutrition and metabolism. The requirements of many plants and animals are listed and the nutrient sources are tabulated. The nutrient and energy values of foods are shown. There are tables of nutrient functions with signs of deficiency and excess. Pathways and end products of metabolism, oxygen consumption, and carbon dioxide production are listed for many plants and animals. The last 13 tables cover energy exchange in several mammals, chickens, and soil organisms.

The tables were compiled by experts and reviewed by specialists. Many of them show not only average figures, but also the range of variation. The data are presented with supplementary information on nomenclature, units, methods, etc. The data are documented by extensive lists of references.

Acute Anuria: A Study Based on Renal Function Tests and Aspiration Biopsy of the Kidney. By Claus Brun. 215 pages. Copenhagen, 1954, Ejnar Munksgaard.

This monograph follows the general pattern of the supplements to the various Scandinavian *Acta*. There is an extensive (49 pages) review of the literature, a detailed description of the material and methods of the study, presentation of results, and an over-all interpretation.

Thirty-two patients with acute renal failure were studied, some superficially and some in detail. Nothing new comes out of the study—the virtue of the monograph is that many published and original data are recorded and integrated. The chief findings are as follows: The majority of deaths result from the precipitating cause of the renal failure rather than from the renal failure itself. The renal tubules lose most of their capacity to concentrate creatinine or urea and to reabsorb sodium. This impairment persists into and through the phase of diuresis. Both glomerular and tubular function, as judged from clearances of inulin and para-aminohippurate, are markedly depressed. There is slow recovery over a period of weeks and even up to six to twelve months. The clearance ratios of inulin increments in whole-body urea point to destruction of body protein, while creatinine increments are less than expected.

Acute renal failure often is attended by mild hypertension, refractory anemia, and urinary tract infection.

Histologic changes include the following: Glomeruli and blood vessels are normal. Hydropic changes and necroses are never localized to the "lower nephron," but sometimes are found exclusively in the proximal tubule. Interstitial changes are prominent and include focal or diffuse edema, often with cellular infiltration of varying intensity.

The Female Sex Hormones. By Leon J. DeMerre. 219 pages. New York, 1954, Vantage Press. $3.50.

The author wrote this book with the intention of informing the ever increasing hormone-conscious lay population about the female endocrines. In this respect the book is of value. Written in nontechnical terms, it has sections on the pituitary gland, estrogens, progesterone, endocrine therapy, lactogenic hormones, sex determination, and homosexuality. Each section is almost a unit in itself. Brief historical notes are included in some chapters. Methods of standardization of hormone units and animal experimentation are discussed.

The reviewer thinks the book satisfactory for some individuals, but wonders if it will be of benefit or hindrance to the average reader. The public may feel that some of their complex problems have too simple a solution. Homosexuals may be led to believe that they act as they do solely because of hormone imbalance and proceed to badger their physicians with requests for testosterone to counterweigh an estrogen excess. Flat-chested women may interpret Dr. DeMerre as implying that the correct combinations of pituitary and ovarian hormones will replace their brassiere pads with voluptuous bosoms.

The writer has attained his purpose but a little knowledge may prove dangerous.

Les Steroids urinaires au cours de la gestation normale et pathologique. Publication des colloques sur la fonction luteale. 131 pages. Paris, 1954, Masson et Cie.

This is a symposium and much of the material has been published elsewhere. *Jayle and Crépy* report that there is no correlation between the urinary excretion of follicular and of luteal hormones. Deficiency of the follicular hormone may precede and cause early or late abortion. Determination of urinary steroids has practical value in indicating substitutional therapy.

Borth found pregnandiol excretion to be decreased in spontaneous abortion. From Guterman's data, he concludes that progesterone administration has a beneficial effect in habitual aborters who have a decreased pregnandiol excretion. In toxemia of pregnancy, the fetal prognosis is bad when the maternal excretion of pregnandiol is decreased.

Huis in't Veld found the excretion of 17-ketosteroids to be increased in normal pregnancy by about 40 per cent over the average in the nonpregnant. Fractionation showed decreased androsterone and etiocholanolone excretion. There were doubled 11-oxyetiocholanolone and 11-hydroxyandrosterone excretions in the first trimester with a drop in the second trimester and increase to 3 times the level in the nonpregnant in the last trimester.

Devis discussed methods for corticoid determinations. When the excretions of corticoids are plotted against duration of pregnancies, normal women show very marked variation.

Simmonet, Piaux, and Robey discuss abortion resulting from deficiencies of follicular or luteal hormones, or both. A few case reports purport to show a beneficial effect of substitution therapy.

Lacomme and Guéguen: Pregnant women previously treated for infertility or who have earlier abortions show a great diversity of abnormalities in urinary steroids. There may be a decreased excretion of follicular or luteal hormones, or both.

Milliez and Fritel: In toxemia of pregnancy the urinary excretion of gonadotrophin is increased but variable. In severe toxemia luteal hormone excretion is rather markedly decreased. Usually the follicular hormone excretion is parallel to the excretion of the luteal hormones, 17-ketosteroids are normal, corticoids relatively increased. There is a disproportion between estrogens and corticoids. Substitutional therapy may prevent toxemic accidents.

Nutritional Status of Mothers and Their Infants. By Elsie Z. Moyer, Harriet J. Kelly, Icie G. Macy, Harold C. Mack, P. C. DiLoreto, and J. P. Pratt. 112 pages, 91 tables. Detroit, 1954, Children's Fund of Michigan.

Three groups of pregnant women were studied: (1) 109 white and 544 Negro women from a public clinic (low income), (2) 33 white and 131 Negro women from a private clinic (moderate income), and (3) 230 white private patients. From these, 160 white and 267 Negro women were selected as "typical" ("normal") to study the effects of pregnancy. The approaches used in the study were: (1) clinical evaluation, (2) qualitative dietary intake records, and (3) serial determinations of hemoglobin, serum proteins, capillary blood levels of vitamin A and C, carotenoids, and alkaline phosphatase. The average hemoglobin, serum protein, and vitamin C levels decreased with progression of the pregnancy, while alkaline phosphatase increased in the last trimester. There was no definite trend in the vitamin A and carotenoid levels. Negro women, on the average, had lower hemoglobin, vitamin A and C, and higher serum protein and alkaline phosphatase levels.

Comparing the newborn infants with their mothers showed the infants to have higher hemoglobin, vitamin C, alkaline phosphatase levels, and lower serum protein, vitamin A, and carotenoid levels.

The 91 tables, which comprise about half of the book, present all observations with many correlations.

Textbook of Operative Gynecology. By Wilfred Shaw. 444 pages with 382 illustrations. Edinburgh and London, 1954, E. & S. Livingstone, Ltd. $19.00.

In the preface of this text, Mr. Shaw states that in recent years many younger British gynecologists have been studying from American and continental textbooks. In an effort to counteract this trend, he has undertaken this work on operative gynecology, the aim of which is to represent British medical publication at its best. Unfortunately, Mr. Shaw did not live to see this publication, but those who will have the pleasure of reading and owning this book will certainly feel that he has achieved his goal.

In keeping with other modern operative texts, this volume is profusely illustrated. The written descriptions of operations, indications, and results are reduced to a minimum. These portions are written for the student who already possesses a knowledge of the subject and not for the medical student. Only the high points are touched. Nevertheless, there can be no mistake regarding the author's opinion and preferences.

There are 29 chapters covering the complete range of operative gynecology, and including sections on preoperative preparation, anesthesia, instruments, needles, techniques, and blood transfusions, and anatomical considerations. Usually more than one operation is given for a specific condition. The illustrations are a little short of superb and speak as much for the author's skill and diligence as they do for the artist's. The bulk of them were done by Mr. Leslie Caswell, a successful commercial artist who has had no anatomical

training and has attended only one or two operative sessions. They were made from photographs and preliminary outline sketches by the author. The results are slightly diagrammatic but while this may distract from their artistic value, it adds to their clarity. Only rarely does it lead to gross distortion as in the illustrations of total hysterectomy (Figs. 41 and 42). No human uterosacral ligaments ever had quite such a fulsome appearance. Really to appreciate the task accomplished one need only look at the illustrations of the Schauta operation. This is a difficult problem to portray and these are far superior to Schauta's own original illustrations.

The only really serious defect in this book is the complete lack of any pathologic anatomy, gross or microscopic. Perhaps if this is intended, as it appears, to be an operative atlas then this lack is not serious.

The format is excellent, the print and printing good, and the reproduction fine. All in all this is an achievement in the art of bookmaking by an author who was a master surgeon, a scholar of breadth, and a lover of fine books.

Klinische Untersuchungen zur Problematik der geburtstraumatischen Schädigung des kindlichen Zentralnervensystems. By Wilhelm H. Thiele. 52 pages. Stuttgart, 1954, Ferdinand Enke. DM9.

This very sensible little book is devoted to a study of the diagnosis, etiology, frequency, and prophylaxis of brain injuries in infants. The author rejects the passage of meconium, fetal bradycardia, and the absence of a strong cry at birth as signs of cerebral trauma. Brain injuries at birth are chiefly the result of bleeding into the brain substance, rather than localized hematomas.

The author feels that the demonstration of corneal opacity immediately after delivery is practically pathognomonic of cerebral trauma. This opacity usually disappears within about forty-eight hours and is due to increased intracranial pressure. It is believed that the principal cause of this intrapartum brain damage is mechanical pressure. The latter occurs in the form of circular pressure about the skull, especially in midpelvis. This results in venous compression and disturbance of arterial supply. If the child survives, he is not likely to demonstrate such serious sequelae as convulsions. Prophylaxis consists largely in the avoidance of all forcible means of conducting labor. Artificial stimulation of the contractions tends to lead to cerebral complications.

Although one can readily take issue with several of the author's points, this is nevertheless a clear and forceful presentation, and, in the main, the ideas expressed are very sound.

Clinical Measurement of Uterine Forces in Pregnancy and Labor. By S. R. M. Reynolds, Jerome S. Harris, and Irwin H. Kaiser. 328 pages, 99 illustrations. Springfield, Ill., 1954, Charles C Thomas. $9.50.

In the introduction to this monograph the authors state that the purpose of their writing is to clarify some of the multitude of impressions and theories of uterine forces as investigated by various methods and, in particular, by internal and external tokodynamometry. Investigators have been publishing data on labor forces for almost two centuries, yet even now there are differences in terminology and procedures used in the research of this problem. The authors attempt to standardize these so that the results of studies in various clinics may be compared.

There are four major sections in the book. The first "Background and Basis," is concerned with the history and physiology of tokometry. The second part, "Methods," describes internal and external tokodynamometry, the analysis of records, and internal uterine pressures during pregnancy and labor. These first two sections will be of interest to those involved in investigation and teaching of uterine actions. The clinician, however, will better understand the results of the findings if he will familiarize himself with

the background of the work. The last two parts are concerned with uterine contractions during pregnancy and labor and the effects of psyche and drugs on uterine contractions. The observations of the authors are supplemented and often correlated with those of Drs. H. Alvarez and R. Caldeyro, who are doing similar studies with internal toko-dynamometers in Uruguay.

The writers have been careful not to become too involved with technical descriptions but are thorough in their explanations. Because of this precision and clarity, reading the book is pleasant as well as informative.

The student of obstetrics reading this book will better understand the dynamics of the expulsive force of the uterus and how this force may be altered by the physician's attitude or by the administration of drugs and anesthetics. Illustrations of records of prodromal, false, and active labor are clear and self-explanatory.

The closing chapter of the book concerns Pitocin. This valuable adjunct to our armamentarium is safe only in the hands of the obstetrician who understands the drug. The authors discuss safety measures in the use of Pitocin, its contraindications, and indications for discontinuance.

The reviewer feels that this monograph is required reading for those involved in the study, teaching, and practice of obstetrics. The knowledge thus acquired will enable them to have a better understanding of the management of the patient in labor.

Correspondence

Different Views as to Pericytoma of the Uterus

To the Editors:

I have read with interest the paper entitled "Hemangiopericytoma of the Uterus" by Drs. Pedowitz, Felmus, and Grayzel, appearing in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, volume 67, page 549, March, 1954.

Having some familiarity with the type of lesion described, I find myself both puzzled and at variance with some of the authors' statements and deductions.

On page 559, one wonders why reference number 12 did not immediately follow the word "stromal" instead of being grouped along with number 13, which seems to refer to "stromatous endometriosis." Another point of ambiguity is found on page 561 in which the words "stromal myosis" appearing in the first sentence would appear to be the antecedent of the word "neoplasm" in the second sentence. If "stromal myosis" and "neoplasm" are synonymous, then "adenomyosis" appearing in the third sentence might just as logically be regarded as something neoplastic, a view with which many would disagree. By their statement that "adenomyosis rarely undergoes malignant degeneration as compared to the greater frequency of such change for 'stromal myosis,'" the authors could mean that adenomyosis is a neoplastic condition. Further, it appears to me that another comparison between "stromal myosis" and adenomyosis contained in the sentence quoted is not a valid one. Adenomyosis of the uterus is a very common entity, as evidenced by the fact that several of my colleagues and I were able to make a study of 1,856 examples in one hospital, whereas the total number of reported instances of stromal endometriosis is still under 100. Is the latter a sufficient number to be valid statistically?

It is difficult, if not impossible, to follow the reasoning and the conclusion in the following sentence (p. 561): "Frank reported a recurrence 17 years after total hysterectomy for 'stromal myosis,' in which the identical pattern of the primary tumor was reproduced, *suggesting an origin from vasoformative cells capable of blood-vessel formation, rather than from stromal cells.*" (Italics mine. W. C. H.) In what way is the element of time a valid criterion as to the cell of origin of "stromal myosis" or any other neoplasm for that matter?

It should also be understood that by no means all competent pathologists accept the existence of a tumor called pericytoma. To me it appears that the authors have placed undue reliance upon the ability of certain stains always to differentiate between various kinds of cells. It is common knowledge that the human factor, variations in the compositions of stains and their preparation, the manner of staining, the fixative employed for the tissue, etc., all conspire to make the experienced pathologist doubt the absolute authenticity of any stain. It would have been of interest to have had the authors compare the so-called "pericytes" of their cases with what all will admit is endometrial stroma as this appears in conjunction with adenomyosis of the uterus and often with ectopic endometriosis elsewhere, or to have compared stromal cells in the immediate vicinity of the spiral arterioles of the endometrium with the presumed "pericytes" around the vessels of their tumors.

WARREN C. HUNTER, M.D.

DEPARTMENT OF PATHOLOGY
UNIVERSITY OF OREGON MEDICAL SCHOOL
PORTLAND, ORE.
OCT. 1, 1954

Reply by Dr. Pedowitz

To the Editors:

My colleagues and I greatly appreciate Dr. Hunter's interest in our paper entitled "Hemangiopericytoma of the Uterus." We fully agree with him that this is still a debatable subject and definitive opinion in regard to this lesion must await further study. Most of the questions raised by Dr. Hunter will be clarified in a forthcoming paper.

His suggestion in regard to the study of the normal endometrial stroma with special stains is well taken and this is being done at the present time.

We wish to thank Dr. Hunter for his excellent criticism and suggestions.

PAUL PEDOWITZ, M.D.

9 PROSPECT PARK WEST
BROOKLYN, N. Y.
OCT. 14, 1954

Various Aspects of Treatment of Trichomonas Vaginalis Vaginitis

To the Editors:

The two papers on *Trichomonas vaginalis* that appeared in the August, 1954, issue of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY were of special interest to me, because I have been conducting a leukorrhea clinic since 1932.

Newer treatments for *Trichomonas vaginalis* are in order, since it has been found that the organism has become resistant to most vaginal and cervical medications used in the past. I now see trichomonads swimming in vaginal preparations which I found to be effective 5 to 15 years ago.

Davis and Grand mentioned the use of a chemical that has the ability to penetrate and to dissolve mucinous material without irritating the already inflamed mucosa, while at the same time it is lethal to the flagellates within three minutes. The use of a spreading agent or agents is absolutely essential in all vaginal medication due to the presence of a "moist layer" that covers the entire vaginal epithelium. It is in this "moist layer" that trichomonads and other pathogenic microorganisms hide during the treatment period. After the treatment is over these pathogens swim back, multiply, and grow, causing a flare-up of the old infestation.

By using an electronic recording pH instrument, we have found that vaginal discharges due to *Trichomonas vaginalis* vary in pH from the bottom to the top of the secretion. The pH may vary from a figure of 4.6 at the bottom to 5.8 at the top. Trichomonads cannot live in the bottom pH 4.6 area, but can live in the pH 4.9 to 5.8 area.

Most nonspreading vaginal medications usually coagulate vaginal discharge, thereby creating a favorable medium for the growth of Trichomonas and other pathogenic microorganisms. Most alkaline vaginal douches also coagulate vaginal leukorrhea. The majority of correctly buffered, correctly acidified douches containing a correct amount of "spreading agent or agents" will dissolve vaginal leukorrhea. There are very few douches, however, which will dissolve cervical leukorrhea. Vaginal douches are not indicated for cervical leukorrhea.

Our clinic has tested over a hundred "spreading agents" and has found that many of them kill *Trichomonas vaginalis* at very low concentrations. At these low concentrations they were not irritating. In a test tube these "spreading agents" were very efficient, but when most of them were placed in the vagina they were found to be inert, since the trichomonads were still active and swimming around as if nothing had been added to the vagina. It has been found that there is no comparison chemically between the test tube with trichomonads in it and trichomonads in a vagina with vaginal secretion. What a chemical or chemicals will do in a test tube and in an infected or normal vagina may vary greatly. Vaginal epithelium and secretions might be compared to a complicated laboratory containing carbohydrates, fats, proteins, enzymes, vitamins, trace elements, minerals, serum, buffers, dilution factor, and the property of forming chemical compounds with added chemicals. The chemicals thus formed may be inert to trichomonads.

It appears that we are trying to use the results of the test-tube studies of chemicals on *Trichomonas vaginalis* instead of using the results of the vaginal-tube studies.

Yet, I believe that there is more to treating *Trichomonas vaginalis* than inserting tablets, insufflating powders, or introducing liquids or jellies into the vagina. There are other considerations, namely: (1) the avoidance of chemicals to which the organisms are resistant; (2) the use of "correctly buffered" acid vaginal preparations; (3) the use of "correctly acidified" preparations; (4) the addition of correct amounts of "spreading agent" or "spreading agents" in vaginal medications; (5) the administration of estrogen. (In trichomonal infestation the vaginal epithelium is in a hypophysiological state. Estrogen stimulates the epithelium and aids in its healing.)

Thus four "hypos" are usually present: hypoacidity; hypobacterial flora (a decrease in the bacterial flora); hypoepithelial cell height; and hypoglycogen. These four factors can be restored to approximately 50 per cent of normal by the giving of estrogen alone. There may be a lack of enough "active" estrogen or insufficient vaginal epithelium to be stimulated by the amount or kind of estrogen present. Estrogen added by mouth or intramuscularly aids in the treatment of Trichomonas vaginitis and other vaginal infections. In acute trichomonal vaginitis in the nonpregnant patient, 100 mg. of micronized vitaminized stilbestrol daily, by mouth, for ten to fourteen days, and 200 to 500 mg. daily in the pregnant patient aid greatly in relieving itching and burning and in correcting the infection. Immediate relief from the signs and symptoms is obtained if the vagina is insufflated with correctly buffered, correctly acidified, spreading-agent powders (Baculin), until the vagina is filled.

Further considerations may also be noted: (6) The knowledge that the patient's daily food intake of proteins, B complex and C vitamins and other vitamins, trace elements, and minerals is essential for normal vaginal epithelial growth, and for the deposition of glycogen within the vagina. These factors also cause the conversion of glycogen within the vaginal epithelium into lactic acid, the normal vaginal acid. The presence of normal amounts of "activated" estrogen is also dependent upon B complex, C, and other vitamins, trace elements, and minerals. Try to keep the patient normal, both physically and mentally by appropriate means.

A knowledge of the sources of infection and reinfection brings me to the next group of considerations: (7) The realization that many women are constantly contaminating their vaginas with fecal matter. Approximately 50 per cent of the women clean to the front after defecation, sweeping fecal matter and bacteria into the vagina which aid in causing vaginitis and cervicitis, and upset the normal physiology of the vagina. (8) The realization that the male is the source of many new and repeated infestations of *Trichomonas vaginalis* as well as reinfection with *Monilia albicans* (fungi) and other pathogenic microorganisms of the vagina and cervix. I have found that trichomonads will die out without treatment in the male in 4 months, if he is not reinfected. If the male wears condoms during coitus for at least 4 months or the wife or sexual partner inserts 4 to 8 correctly buffered, acidified, spreading-agent tablets into the vagina immediately following coitus, the microorganisms of the vagina and cervix will be destroyed in most instances. (9) The instruction of the patients in how to prevent recurrences after the infection is eradicated. The patient should insert 2 correctly buffered, acidified, spreading-agent tablets into the vagina 3 times daily as soon as the slighest amount of itching, burning, or discharge recurs. This treatment should be maintained for four to seven days. This regimen will stop most reinfection before it can become reestablished in the vagina. (10) The immediate treatment of the vagina during the first menstrual period after the diagnosis is made. I have never seen trichomonads undergoing cell division except during menstruation or in the presence of serum, as in the case of vaginitis. A woman may obtain several trichomonads at coitus. This number may remain the same or decrease; but during the menstrual flow growth and multiplication will occur, and several million trichomonads may result. I believe that one of the main reasons that trichomonads recur is that treatment is stopped during the menstrual period, the time of most avid trichomonal reproduction. The vagina should be cleaned of all menstrual fluid and the entire vaginal vault filled with correctly buffered, acidified, spreading-agent powders on at

least one day of the menstrual cycle. (11) Trichomonads may live in the infected cervix during the treatment period, and, after the treatment is discontinued, may reinfect the vagina. Trichomonads may also live in ulcers of the vaginal epithelium, or in the labia, Skene's ducts, Bartholin's glands, and the bladder. From these numerous foci they may easily reinfect the vagina. Contaminated towels, bathtubs, and douche nozzles are also sources of infection. (12) The addition of a fungicide, trichomonacide, and a bactericide in the vaginal and cervical preparation is essential. To illustrate: If the fungicide is omitted from the preparation, a fungus condition worse than the original infection may be produced. This unfortunate circumstance has occurred too many times in our clinic.

(13) The adequate testing of any new vaginal preparation in a sufficient number of cases and over a sufficiently long period of time to determine exact results is always important. Over 50 per cent of trichomonal vaginal infestations are easily amenable to most treatments. If one treated 50 cases of trichomonads which are easily amenable to treatment with a new medication, then one might falsely assume that the new medication is a better preparation. Another group of important considerations is related to techniques of detection. (14) The employment of a technician who is trained in the recognition of *Trichomonas vaginalis* is essential. I have had registered technicians who could recognize a microscopic field covered with trichomonads, but if only a few were present they would be missed. Essential technical steps in demonstrating the organism include: (a) the obtaining of a sufficient amount of secretion from the vagina with two cotton applicators; (b) the placing of the vaginal smear on the cotton applicators into a test tube containing 0.5 c.c. of normal saline, followed by the immersion of this tube in a water bath at body temperature (if the smear is too diluted the chance of finding trichomonads is greatly diminished); (c) the spreading of this saline-secretion mixture in a thick smear across the entire length of a clean, plain slide.

(15) Certain steps in therapy must be carefully avoided, namely: (a) The ill-advised use of alkaline or very weak acid medications which favor the growth of trichomonads. (b) The grossly incorrect use of plain water douches. Many patients have admitted using plain water douches while bathing, yet they were told not to douche. A plain water douche appears to wash out the glycogen in the epithelium more readily than do acidic douches, and I feel that no douche at all is better than a plain water douche. (c) The use of unphysiological, unbuffered, nonspreading, ineffectually acidic vaginal douches which tend to lower the resistance of the vaginal epithelium.

Finally, there remains the constant perserverance necessary to unearth the multitude of fascinating facts which still remain the hidden secrets of the elusive trichomonads.

KARL JOHN KARNAKY, M.D.

329 MEDICAL ARTS BUILDING
HOUSTON 2, TEXAS
OCT. 17, 1954.

Items

American Board of Obstetrics and Gynecology

The next scheduled examination (Part I), written examination and review of case histories, for all candidates will be held in various cities of the United States, Canada, and military centers outside the continental United States, on Friday, Feb. 4, 1955.

Case Abstracts numbering 20 are to be sent by the candidate to the Secretary as soon as possible after receiving notification of eligibility to the Part I written examination.

ROBERT L. FAULKNER, M.D., SECRETARY
2105 ADELBERT ROAD
CLEVELAND 6, OHIO

Fourteenth British Congress of Obstetrics and Gynaecology

The Fourteenth British Congress of Obstetrics and Gynaecology will be held in Oxford, England, July 27-30, 1955. For information write to

THE CONGRESS SECRETARIES
RADCLIFFE INFIRMARY
OXFORD, ENGLAND

Arkansas Obstetrical and Gynecological Society

The fall meeting of The Arkansas Obstetrical and Gynecological Society was held in Little Rock on Oct. 22 and 23, 1954, with the Memphis and Mississippi Societies as guests. There were 75 doctors in attendance.

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January and July)

American Academy of Obstetrics and Gynecology. (1945) *President,* Bayard Carter. *Secretary,* C. Paul Hodgkinson, 17546 Meadowood Ave., Lathrup Village, Birmingham, Mich.

American Gynecological Society. (1876) *President,* Philip F. Williams. *Secretary,* John I. Brewer, 104 S. Michigan Ave., Chicago 3, Ill. Next meeting, Chateau Frontenac, Quebec, Canada, May 23, 24, and 25, 1955.

American Association of Obstetricians and Gynecologists. (1888) *President,* Thaddeus L. Montgomery. *Secretary,* Frank R. Lock, Bowman Gray School of Medicine, Winston-Salem, N. C. Annual meeting at Hot Springs, Va., Sept. 8, 9, and 10, 1954.

Central Association of Obstetricians and Gynecologists. (1929) *President,* Frank L. McPhail. *Secretary,* Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Ill. Annual meeting at Columbus, Ohio, Oct. 6, 7, and 8, 1955.

South Atlantic Association of Obstetricians and Gynecologists. (1938) *President,* Robert G. Nelson. *Secretary,* Charles H. Mauzy, Bowman Gray School of Medicine, Winston-Salem, N. C. Next meeting, Williamsburg Inn and Lodge, Williamsburg, Va., Feb. 10, 11, and 12, 1955.

A. M. A. Section on Obstetrics and Gynecology. *Chairman,* Frederick H. Falls, *Secretary,* D. Frank Kaltreider, University Hospital, Baltimore 1, Md. Next meeting, Atlantic City, N. J., June 6-10, 1955.

Society of Obstetricians and Gynaecologists of Canada. (1944) *President,* A. M. Agnew, *Secretary,* F. P. McInnis, 1230 Avenue Road, Toronto, Ont. Next meeting, Bigwin Inn, Muskoka, Ont., June 17, 18, and 19, 1955.

Akron Obstetrical and Gynecological Society. (1946) *President,* Norman E. Wentsler. *Secretary,* Charles V. Bowen, Jr., 925 Second National Bldg., Akron 8. Meetings, third Friday of month, October, January, April, and July.

Alabama Association of Obstetricians and Gynecologists. (1940) *President,* Thomas B. Woods, Dothan. *Secretary,* James H. French, 201 Montgomery St., Montgomery. Next meeting, April 20, 1955, in Montgomery.

Alameda County Gynecological Society. (1951) *President,* Charles Lewis. *Secretary,* Wilson Footer, 2828 Summit St., Oakland 9, Calif. Meetings, fourth Wednesday of each month except July, August, and December.

Arkansas Obstetrical and Gynecological Society. (1953) *President,* Charles R. Wickard, Little Rock. *Secretary,* J. F. Kelsey, Fort Smith. Meetings, spring and fall.

Atlanta Obstetrical and Gynecological Society. (1954) *President,* R. A. Bartholomew. *Secretary,* George A. Williams, Suite 6, 710 Peachtree St., N. E., Atlanta 5, Ga. Meetings quarterly.

Birmingham Obstetrical and Gynecological Society. (1949) *President,* S. U. Newfield. *Secretary,* Julian P. Hardy, 920 S. 19th St., Birmingham. Meetings, second Thursday of month, January, March, September, and November.

Boston, Obstetrical Society of. (1861) *President,* Arthur T. Hertig. *Secretary,* A. Gordon Gauld, 1180 Beacon St., Brookline 46, Mass. Meetings, third Tuesday of October, November, January, February, and March. Tri-city meeting, third Tuesday of April.

Bronx Gynecological and Obstetrical Society. (1924) *President,* John S. Labate. *Secretary,* Sol S. Schifrin, 930 Grand Concourse, New York 51, N. Y. Meetings, fourth Monday, October, November, January, February, March, April, and May.

Brooklyn Gynecological Society. (1890) *President,* William Levine. *Secretary,* Leslie H. Tisdall, 615 Third St., Brooklyn 15. Meetings, third Wednesday, October, November, January, February, March, April, and May.

Buffalo Obstetrical and Gynecological Society. (1946) *President,* Lewis McLean. *Secretary,* Louis A. Trippe, 511 Lafayette Ave., Buffalo 22, N. Y. Meetings, first Tuesday, October through May.

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*Changes, omissions, and corrections should be sent to the publisher, The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, Mo. The number after the Society's name is the year of founding. For further information, address the respective secretaries.

Central New York Association of Gynecologists and Obstetricians. (1938) *President,* J. Loder, Rochester. *Secretary,* William Redfield, State Tower Bldg., Syracuse. Meetings, third Tuesday, January, March, May, and October.

Chicago Gynecological Society. (1878) *President,* J. P. Greenhill. *Secretary,* Clyde J. Geiger, 4753 Broadway, Chicago 40. Meetings, third Friday, October through June.

Cincinnati Obstetrical Society. (1876) *President,* Richard D. Bryant. *Secretary,* John F. Mohan, 3731 St. Lawrence, Cincinnati. Meetings, third Thursday, September through May.

Cleveland Society of Obstetrics and Gynecology. (1947) *President,* A. C. Siddall. *Secretary,* Eduard Eichner, 10605 Chester Ave., Cleveland 6. Meetings, fourth Monday, September, November, January, March, and May.

Columbus Obstetric-Gynecologic Society. (1944) *President,* Anthony Ruppersberg, Jr. *Secretary,* Fred B. Hapke, 350 E. Broad St., Columbus 15. Meetings, last Wednesday of month, September through May.

Dallas-Fort Worth Obstetrical and Gynecological Society. (1948) *President,* Hugh Savage. *Secretary,* H. I. Kantor, 3534 Maple Ave., Dallas. Meetings, spring and fall.

Denver Gynecological and Obstetrical Society. (1942) *President,* John R. Evans. *Secretary,* Raymond C. Chatfield, 1809 E. 18th Ave., Denver 18, Colo. Meetings, first Monday of every month, unless otherwise notified.

El Paso County Obstetrical and Gynecological Society. (1948) *President,* Erich Spier. *Secretary,* Alvin L. Perry, 209 Medical Arts Bldg., El Paso, Texas. Meetings, last Thursday, every other month.

Florida Obstetric and Gynecologic Society. (1948) *President,* Harold G. Nix. *Secretary,* R. B. Chrisman, Jr., 743 duPont Bldg., Miami. Meetings, December and April.

Georgia State Obstetrical and Gynecological Society. (1951) *President,* Albert J. Kelly. *Secretary,* Eugene L. Griffin, 26 Linden Ave., N. E., Atlanta. Next meeting, Augusta, May 1-4, 1955.

Harris, John Warton, Obstetrical Society. (1953) *President,* E. Russell Muntz. *Secretary,* Alice D. Watts, 324 E. Wisconsin Ave., Milwaukee 2, Wis. Meeting, Sept. 3 and 4, 1955.

Honolulu Obstetrical and Gynecological Society. (1947) *President,* James T. S. Wong. *Secretary,* Fugate Carty, Straub Clinic, Thomas Square, Honolulu. Meetings, third Monday of each month at the Mabel Smyth Memorial Bldg.

Houston Obstetrical and Gynecological Society. (1939) *President,* J. A. Clapp, Jr. *Secretary,* Murphy D. Stevenson, 807 Hermann Professional Bldg., Houston. Meetings, first Tuesday each month, October through June.

Indianapolis Obstetrical and Gynecological Society. (1947) *President,* Alexander Cavins. *Secretary,* Paul F. Muller, 3311 N. Meridian St., Indianapolis. Meetings, second Wednesday in January, May, and October.

Interurban Obstetrical and Gynecological Society. (1949) *President,* Fred Fumia, Rochester, N. Y. *Secretary,* E. R. Duggan, 16 N. Goodman St., Rochester 7, N. Y. Meeting, October, 1955.

Iowa Obstetrical and Gynecological Society. *President,* Parker K. Hughes. *Secretary,* William C. Keettel, State University of Iowa Hospitals, Iowa City. Meetings, spring and fall.

Kansas City Gynecological Society. (1922) *President,* Leroy A. Calkins. *Secretary,* James E. Keeler, 4301 Main St., Kansas City, Mo. Meetings, third Thursday, September, November, January, and March, and first Thursday in May.

Kentucky Obstetrical and Gynecological Society. (1947) *President,* J. B. Marshall, Louisville. *Secretary,* R. C. Bateman, 432 W. Main St., Danville. Annual meeting, Louisville, March 31-April 3, 1955.

Los Angeles Obstetrical and Gynecological Society. (1914) *President,* A. N. Webb. *Secretary,* Ralph Walker, 10711 Riverside Drive, North Hollywood, Calif. Meetings, second Tuesday, September, November, January, March, and May.

Louisville Obstetrical and Gynecological Society. *President,* William E. Oldham. *Secretary,* V. E. Masters, 517 Fincastle Bldg., Louisville 2. Meetings, fourth Monday, September, October, November, January, February, March, April, and May.

Madison Obstetrical and Gynecological Society. (1950) *President* and *Secretary,* Lee B. Stevenson, 16 S. Henry St., Madison 3, Wis. Meetings, first Tuesday each month except July, August, and September.

Maryland, Obstetrical and Gynecological Society of. (1929) *President,* Everett S. Diggs. *Secretary,* Harry M. Beck, 700 N. Charles St., Baltimore 1. Meetings, second Thursday, October, December, February, and April.

Memphis Obstetrical and Gynecological Society. (1950) *President,* Nate Atherton. *Secretary,* William F. Mackey, 1374 Madison Ave., Memphis, Tenn. Meetings, second Tuesday, November, December, January, March, and May.

Miami Obstetrical and Gynecological Society. (1946) *President,* Norman McLeod. *Secretary,* Richard C. Forman, 427 Biltmore Way, Coral Gables. Meetings, second Thursday, January, March, May, and November.

Michigan Society of Obstetricians and Gynecologists. (1924) *President,* R. L. Haas. *Secretary,* C. Paul Hodgkinson, 2799 W. Grand Blvd., Detroit 2. Meetings, first Tuesday, October, November, December, February, March, April, and May.

Minnesota Obstetrical and Gynecological Society. *President,* Arnold O. Swenson, Duluth. *Secretary,* Rodney F. Sturley, 350 Saint Peter St., St. Paul. Meetings, spring and fall.

Mississippi Obstetrical and Gynecological Society. (1947) *President,* Claude G. Callender, Jackson. *Secretary,* J. A. K. Birchett, Jr., The Street Clinic, Vicksburg. Meetings May and October.

Mobile County Obstetrical and Gynecological Society. (1949) *President,* H. B. Dowling. *Secretary,* J. R. Mighell, 1302 Government St., Mobile. Meetings, quarterly when called.

Montgomery County (Ohio) Obstetrical and Gynecological Society. (1937) *President,* L. O. Fredericks. *Secretary,* A. A. Kunnen, 406 Harries Bldg., Dayton, Ohio. Meetings, third Wednesday of each month.

Montana Obstetrical and Gynecological Society. (1946) *President,* Harold W. Fuller, Great Falls. *Secretary,* Leonard W. Brewer, 212 N. Higgins Ave., Missoula.

Nassau Obstetrical Society. (1944) *President,* Richard L. Jones. *Secretary,* George E. Christmann, 1502 Mott Avenue, Far Rockaway, N. Y. Meetings, second Monday, October, December, February, and April.

New England Obstetrical and Gynecological Society. (1929) *President,* Edward F. Shay. *Secretary,* Carmi R. Alden, 270 Commonwealth Ave., Boston 16, Mass.

New Haven Obstetrical and Gynecological Society. (1946) *President,* Harry Conte. *Secretary,* Fred Gibson, 315 Whitney Ave., New Haven, Conn. Meetings, third Tuesday, September, November, January, March, and May.

New Jersey Obstetrical and Gynecological Society. (1947) *President,* John D. Preece, Trenton. *Secretary,* Paul Grossbard, 162 Lexington Ave., Passaic. Meetings, October and April.

New Mexico Obstetrical and Gynecological Society. (1947) *President,* W. O. Connor. *Secretary,* A. C. Rood, 6 Medical Arts Square, Albuquerque. Meetings, quarterly.

New Orleans Gynecological and Obstetrical Society. (1924) *President,* John C. Weed. *Secretary,* Abe Mickal, 1413 Richards Bldg., New Orleans. Meetings, October, November, January, March, and May.

New York Obstetrical Society. (1863) *President,* Charles M. McLane. *Secretary,* Henry S. Acken, Jr., 34 Prospect Park West, Brooklyn 15. Meetings, second Tuesday, October through May.

North Carolina Obstetrical and Gynecological Society. (1932) *President,* Richard L. Pearse, Durham. *Secretary,* Adam Thorp, Rocky Mount. Meeting last weekend in April, 1954.

North Dakota Society of Obstetrics and Gynecology. (1938) *President,* C. M. Lund. *Secretary,* John Gillam, Box 1388, Fargo. Meetings, spring and fall.

Northeastern New York Obstetrical and Gynecological Society. (1935) *President,* William Mallia. *Secretary,* Alton J. Spencer, 42 Division St., Amsterdam, N. Y. Meetings, third Thursday of January, April, and October.

Oklahoma City Obstetrical and Gynecological Society. (1940) *President,* Delbert G. Smith. *Secretary,* Daisy G. Cotten, 525 N. W. 11th St., Oklahoma City. Meetings, February 9, April 13, May 5, 1955.

Omaha Obstetrical and Gynecological Society. (1947) *President,* Donald C. Vroman. *Secretary,* W. Riley Kovar, 1120 Medical Arts Bldg., Omaha 2. Meetings, third Wednesday, January, March, May, September, and November.

Oregon Society of Obstetricians and Gynecologists. *President,* Ronald Neilson. *Secretary,* Alfred N. Marshall, 310 Selling Bldg., Portland 5. Meetings, third Friday, October through May, except December.

Pacific Coast Obstetrical and Gynecological Society. (1931) *President,* Henry A. Stephenson. *Secretary,* Donald W. DeCarle. Meeting, The Lodge, Sun Valley, Idaho, Oct. 6-9, 1955.

Pacific Northwest Obstetrical and Gynecological Association. (1947) *President,* J. E. Harrison. *Secretary,* Earl L. Hall, 1220 Central Ave., Great Falls, Mont. Meeting, Empress Hotel, Victoria, B. C., May 15-18, 1955.

Philadelphia, Obstetrical Society of. (1868) *President,* J. Robert Willson. *Secretary,* Paul A. Bowers, 2031 Locust St., Philadelphia 3, Pa. Meetings, first Thursday, October through May.

Pittsburgh Obstetrical and Gynecological Society. (1934) *President,* R. Charles Nucci. *Secretary,* John C. Hughes, Schenley Park Apts., Pittsburgh 13, Pa. Meetings, first Monday, October through May, except January.

Portland Society of Obstetricians and Gynecologists. (1928) *President,* Kenneth J. Scales. *Secretary,* Gerald E. Kinzel, Medical Dental Bldg., Portland 5, Oregon. Meetings, fourth Wednesday, September through May.

Queens Gynecological Society. (1948) *President,* Daniel B. Langley. *Secretary,* Joseph A. Gaetane, 147-15 46th Ave., Flushing, N. Y. Meetings, second Wednesday, October, December, February, and April.

Rochester Obstetrical and Gynecological Society. (1939) *President,* Louis Iuppa. *Secretary,* Fred Fumia, 39 N. Goodman St., Rochester, N. Y. Meetings, September, December, March, and June.

St. Louis Gynecological Society. (1924) *President,* Willard M. Allen. *Secretary,* Eugene G. Hamilton, 8505 Delmar Blvd., St. Louis 24. Meetings, second Thursday, October, December, February, and April.

San Antonio Obstetrical and Gynecological Society. *President,* G. G. Passmore. *Secretary,* Frank M. Posey, Jr., 640 Moore Bldg. Meetings, first Monday of the month.

San Diego Gynecological Society. (1937) *President,* James Ravenscroft. *Secretary,* Wayne B. Henderson, 2109 5th Ave., San Diego, Calif. Meetings, second Monday of each month.

San Francisco Gynecological Society. (1929) *President,* James V. Campbell. *Secretary,* Edmund F. Anderson, 2445 Ocean Ave., San Francisco 27, Calif. Meetings, second Friday, October through April.

Seattle Gynecological Society. (1941) *President,* C. S. Fine. *Secretary,* John Clancy, 1010 Boylston, Seattle, Wash. Meetings, third Wednesday of each month, except summer months.

South Carolina Obstetrical and Gynecological Society. (1946) *President,* Frank B. C. Geibel. *Secretary,* Lawrence L. Hester, Jr., 16 Lucas St., Charleston 16. Meeting, spring.

Southwest Obstetrical and Gynecological Society. (1951) *President,* Celso C. Stapp, El Paso, Texas. *Secretary,* Zeph B. Campbell, 15 E. Monroe St., Phoenix, Ariz. Annual meeting, fall.

Texas Association of Obstetricians and Gynecologists. (1930) *President,* G. F. Goff. *Secretary,* Carey Hiett, 815 Fifth Ave., Ft. Worth. Annual meeting in February.

Utah Obstetrical and Gynecological Society. (1948) *President,* M. S. Sanders. *Secretary,* Von G. Holbrook, 508 East South Temple, Salt Lake City 2. Meetings, to be announced.

Virginia Obstetrical and Gynecological Society. (1936) *President,* Eugene S. Groseclose, Lynchburg. *Secretary,* Chester D. Bradley, 2914 West Ave., Newport News. Meetings, April and October.

Washington Gynecological Society. (1933) *President,* Raymond Holden. *Secretary,* James Dusbabek, 1801 K St., N. W., Washington, D. C. Meetings, October, December, January, March, and May.

Washington State Obstetrical Association. (1936) *President,* Richard R. Reekie, Spokane. *Secretary,* Robert Campbell, 805 Medical Dental Bldg., Seattle 1. Next meeting, Multnomah Hotel, Portland, Ore., March 26, 1955.

West Texas Obstetrical and Gynecological Society. (1954) *President,* Jesse N. Burditt, Abilene. *Secretary,* D. D. Wall, 234 W. Beauregard Ave., San Angelo. Meetings, twice yearly.

Wisconsin Society of Obstetrics and Gynecology. (1940) *President,* George S. Kilkenny. *Secretary,* Dean D. Willson, 92 East Division St., Fond du Lac. Meetings, May and October.